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| (57) Abstract The invention disclosed in this patent document relates to transmembrane receptors, more particularly to endogenous, human orphan G protein-coupled receptors. | | | |

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HUMAN ORPHAN G PROTEIN-COUPLED RECEPTORS

This patent document claims priority benefit of each of the following applications, all filed with the United States Patent and Trademark Office via U.S. Express Mail on the indicated filing dates: U.S. Provisional Number 60/121,852, filed; February 26, 1999 claiming the benefit of U.S. Provisional Number 60/109,213, filed November 20, 1998; U.S. Provisional Number 60/120,416, filed February 16, 1999; U.S. Provisional Number 60/123,946, filed March 12, 1999; U.S. Provisional Number 60/123,949, filed March 12, 1999; U.S. Provisional Number 60/136,436, filed May 28, 1999; U.S. Provisional Number 60/136,439, filed May 28, 1999; U.S. Provisional Number 60/136,567, filed May 28, 1999; U.S. Provisional Number 60/137,127, filed May 28, 1999; U.S. Provisional Number 60/137,131, filed May 28, 1999; U.S. Provisional Number 141,448, filed June 29, 1999 claiming priority from U.S. Provisional Number 60/136,437, filed May 28, 1999; U.S. Provisional Number _____ (Arena Pharmaceuticals, Inc. docket number CHN10-1), filed September 29, 1999; U.S. Provisional Number 60/156,333, filed September 29, 1999; U.S. Provisional Number 60/156,555, filed September 29, 1999; U.S. Provisional Number 60/156,634, filed September 29, 1999; U.S. Provisional Number _____ (Arena Pharmaceuticals, Inc. docket number RUP6-1), filed October 1, 1999; U.S. Provisional Number _____ (Arena Pharmaceuticals, Inc. docket number RUP7-1), filed October 1, 1999; U.S. Provisional Number _____ (Arena Pharmaceuticals, Inc. docket number CHN6-1), filed October 1, 1999; U.S. Provisional

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Number _____ (Arena Pharmaceuticals, Inc. docket number RUP5-1), filed October 1, 1999; U.S. Provisional Number _____ (Arena Pharmaceuticals, Inc. docket number CHN9-1), filed October 1, 1999. This patent document is related to U.S. Serial Number 09/170,496 filed October 13, 1998, and U.S. Serial Number unknown (Woodcock Washburn Kurtz Mackiewicz & Norris, LLP docket number AREN-0054) filed on October 12, 1999 (via U.S. Express Mail) both being incorporated herein by reference. This patent document also is related to U.S. Serial No. 09/364,425; filed July 30, 1999, which is incorporated by reference in its entirety. This application also claims priority to U.S. Serial Number _____ (Woodcock, Washburn, Kurtz, Makiewicz & Norris, LLP docket number AREN-0050), filed on October 12, 1999 (via U.S. Express Mail), incorporated by reference herein in its entirety. Each of the foregoing applications are incorporated herein by reference in their entirety.

FIELD OF THE INVENTION

The invention disclosed in this patent document relates to transmembrane receptors, and more particularly to endogenous, orphan, human G protein-coupled receptors ("GPCRs").

BACKGROUND OF THE INVENTION

Although a number of receptor classes exist in humans, by far the most abundant and therapeutically relevant is represented by the G protein-coupled receptor (GPCR or GPCRs) class. It is estimated that there are some 100,000 genes within the human genome, and of these, approximately 2% or 2,000 genes, are estimated to code for GPCRs. Receptors, including GPCRs, for which the endogenous ligand has been identified are referred to as "known" receptors, while receptors for which the endogenous ligand has not been identified

are referred to as "orphan" receptors. GPCRs represent an important area for the development of pharmaceutical products: from approximately 20 of the 100 known GPCRs, 60% of all prescription pharmaceuticals have been developed. This distinction is not merely semantic, particularly in the case of GPCRs. Thus, the orphan GPCRs are to the pharmaceutical industry what gold was to California in the late 19th century – an opportunity to drive growth, expansion, enhancement and development.

GPCRs share a common structural motif. All these receptors have seven sequences of between 22 to 24 hydrophobic amino acids that form seven alpha helices, each of which spans the membrane (each span is identified by number, *i.e.*, transmembrane-1 (TM-1), transmembrane-2 (TM-2), etc.). The transmembrane helices are joined by strands of amino acids between transmembrane-2 and transmembrane-3, transmembrane-4 and transmembrane-5, and transmembrane-6 and transmembrane-7 on the exterior, or "extracellular" side, of the cell membrane (these are referred to as "extracellular" regions 1, 2 and 3 (EC-1, EC-2 and EC-3), respectively). The transmembrane helices are also joined by strands of amino acids between transmembrane-1 and transmembrane-2, transmembrane-3 and transmembrane-4, and transmembrane-5 and transmembrane-6 on the interior, or "intracellular" side, of the cell membrane (these are referred to as "intracellular" regions 1, 2 and 3 (IC-1, IC-2 and IC-3), respectively). The "carboxy" ("C") terminus of the receptor lies in the intracellular space within the cell, and the "amino" ("N") terminus of the receptor lies in the extracellular space outside of the cell.

Generally, when an endogenous ligand binds with the receptor (often referred to as "activation" of the receptor), there is a change in the conformation of the intracellular region that allows for coupling between the intracellular region and an intracellular "G-protein." It

has been reported that GPCRs are "promiscuous" with respect to G proteins, *i.e.*, that a GPCR can interact with more than one G protein. *See*, Kenakin, T., 43 *Life Sciences* 1095 (1988). Although other G proteins exist, currently, Gq, Gs, Gi, and Go are G proteins that have been identified. Endogenous ligand-activated GPCR coupling with the G-protein begins a signaling cascade process (referred to as "signal transduction"). Under normal conditions, signal transduction ultimately results in cellular activation or cellular inhibition. It is thought that the IC-3 loop as well as the carboxy terminus of the receptor interact with the G protein.

Under physiological conditions, GPCRs exist in the cell membrane in equilibrium between two different conformations: an "inactive" state and an "active" state. A receptor in an inactive state is unable to link to the intracellular signaling transduction pathway to produce a biological response. Changing the receptor conformation to the active state allows linkage to the transduction pathway (via the G-protein) and produces a biological response. A receptor may be stabilized in an active state by an endogenous ligand or a compound such as a drug.

SUMMARY OF THE INVENTION

Disclosed herein are human endogenous orphan G protein-coupled receptors.

BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1A and 1B provide reference "grids" for certain dot-blot analyses provided herein (see also, Figure 2A and 2B, respectively).

Figures 2A and 2B provide reproductions of the results of certain dot-blot analyses resulting from hCHN3 and hCHN8, respectively (see also, Figures 1A and 1B, respectively).

Figure 3 provides a reproduction of the results of RT-PCR analysis of hRUP3.

Figure 4 provides a reproduction of the results of RT-PCR analysis of hRUP4.

Figure 5 provides a reproduction of the results of RT-PCR analysis of hRUP6.

DETAILED DESCRIPTION

The scientific literature that has evolved around receptors has adopted a number of terms to refer to ligands having various effects on receptors. For clarity and consistency, the following definitions will be used throughout this patent document. To the extent that these definitions conflict with other definitions for these terms, the following definitions shall control:

AMINO ACID ABBREVIATIONS used herein are set out in Table 1:

| 10 | TABLE 1 | | |
|----|---------------|-----|---|
| | ALANINE | ALA | A |
| | ARGININE | ARG | R |
| | ASPARAGINE | ASN | N |
| | ASPARTIC ACID | ASP | D |
| 15 | CYSTEINE | CYS | C |
| | GLUTAMIC ACID | GLU | E |
| | GLUTAMINE | GLN | Q |
| | GLYCINE | GLY | G |
| | HISTIDINE | HIS | H |
| 20 | ISOLEUCINE | ILE | I |
| | LEUCINE | LEU | L |
| | LYSINE | LYS | K |
| | METHIONINE | MET | M |
| | PHENYLALANINE | PHE | F |
| 25 | PROLINE | PRO | P |
| | SERINE | SER | S |
| | THREONINE | THR | T |
| | TRYPTOPHAN | TRP | W |
| | TYROSINE | TYR | Y |
| 30 | VALINE | VAL | V |

COMPOSITION means a material comprising at least one component.

ENDOGENOUS shall mean a material that a mammal naturally produces.

ENDOGENOUS in reference to, for example and not limitation, the term "receptor," shall mean that which is naturally produced by a mammal (for example, and not limitation, a

human) or a virus. By contrast, the term **NON-ENDOGENOUS** in this context shall mean that which is not naturally produced by a mammal (for example, and not limitation, a human) or a virus.

HOST CELL shall mean a cell capable of having a Plasmid and/or Vector incorporated therein. In the case of a prokaryotic Host Cell, a Plasmid is typically replicated as an autonomous molecule as the Host Cell replicates (generally, the Plasmid is thereafter isolated for introduction into a eukaryotic Host Cell); in the case of a eukaryotic Host Cell, a Plasmid is integrated into the cellular DNA of the Host Cell such that when the eukaryotic Host Cell replicates, the Plasmid replicates. Preferably, for the purposes of the invention disclosed herein, the Host Cell is eukaryotic, more preferably, mammalian, and most preferably selected from the group consisting of 293, 293T and COS-7 cells.

LIGAND shall mean an endogenous, naturally occurring molecule specific for an endogenous, naturally occurring receptor.

NON-ORPHAN RECEPTOR shall mean an endogenous naturally occurring molecule specific for an endogenous naturally occurring ligand wherein the binding of a ligand to a receptor activates an intracellular signaling pathway.

ORPHAN RECEPTOR shall mean an endogenous receptor for which the endogenous ligand specific for that receptor has not been identified or is not known.

PLASMID shall mean the combination of a Vector and cDNA. Generally, a Plasmid is introduced into a Host Cell for the purposes of replication and/or expression of the cDNA as a protein.

VECTOR in reference to cDNA shall mean a circular DNA capable of incorporating at least one cDNA and capable of incorporation into a Host Cell.

The order of the following sections is set forth for presentational efficiency and is not intended, nor should be construed, as a limitation on the disclosure or the claims to follow.

Identification of Human GPCRs

5 The efforts of the Human Genome project have led to the identification of a plethora of information regarding nucleic acid sequences located within the human genome; it has been the case in this endeavor that genetic sequence information has been made available without an understanding or recognition as to whether or not any particular genomic sequence does or may contain open-reading frame information that translate human proteins.

10 Several methods of identifying nucleic acid sequences within the human genome are within the purview of those having ordinary skill in the art. For example, and not limitation, a variety of GPCRs, disclosed herein, were discovered by reviewing the GenBank™ database, while other GPCRs were discovered by utilizing a nucleic acid sequence of a GPCR, previously sequenced, to conduct a BLAST™ search of the EST database. Table A, below,

15 lists the disclosed endogenous orphan GPCRs along with a GPCR's respective homologous GPCR:

TABLE A

| | Disclosed | Accession | Open Reading | Per Cent | Reference To |
|----|-----------|------------|--------------|---------------|-----------------|
| | Human | Number | Frame | Homology | Homologous |
| 20 | Orphan | Identified | (Base Pairs) | To Designated | GPCR |
| | GPCRs | | | GPCR | (Accession No.) |
| | hARE-3 | AL033379 | 1,260 bp | 52.3% LPA-R | U92642 |
| | hARE-4 | AC006087 | 1,119 bp | 36% P2Y5 | AF000546 |

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| | | | | | |
|----|--------|-------------|----------|----------------------|-----------|
| | hARE-5 | AC006255 | 1,104 bp | 32% <i>Oryzias</i> | D43633 |
| | | | | <i>latipes</i> | |
| | hGPR27 | AA775870 | 1,128 bp | | |
| | hARE-1 | AI090920 | 999 bp | 43% | D13626 |
| | | | | KIAA0001 | |
| 5 | hARE-2 | AA359504 | 1,122 bp | 53% GPR27 | |
| | hPPR1 | H67224 | 1,053 bp | 39% EBI1 | L31581 |
| | hG2A | AA754702 | 1,113 bp | 31% GPR4 | L36148 |
| | hRUP3 | AL035423 | 1,005 bp | 30% | 2133653 |
| | | | | <i>Drosophila</i> | |
| | | | | <i>melanogaster</i> | |
| | hRUP4 | AI307658 | 1,296 bp | 32% pNPGPR | NP_004876 |
| | | | | 28% and 29 % | AAC41276 |
| | | | | <i>Zebra fish</i> Ya | and |
| | | | | and Yb, | AAB94616 |
| | hRUP5 | AC005849 | 1,413 bp | respectively | |
| | | | | 25% DEZ | Q99788 |
| | | | | 23% FMLPR | P21462 |
| 10 | hRUP6 | AC005871 | 1,245 bp | 48% GPR66 | NP_006047 |
| | hRUP7 | AC007922 | 1,173 bp | 43% H3R | AF140538 |
| | hCHN3 | EST 36581 | 1,113 bp | 53% GPR27 | |
| | hCHN4 | AA804531 | 1,077 bp | 32% thrombin | 4503637 |
| | hCHN6 | EST 2134670 | 1,503 bp | 36% edg-1 | NP_001391 |
| 15 | hCHN8 | EST 764455 | 1,029 bp | 47% | D13626 |
| | | | | KIAA0001 | |
| | hCHN9 | EST 1541536 | 1,077 bp | 41% LTB4R | NM_000752 |
| | hCHN10 | EST 1365839 | 1,055 bp | 35% P2Y | NM_002563 |

Receptor homology is useful in terms of gaining an appreciation of a role of the disclosed receptors within the human body. Additionally, such homology can provide insight 20 as to possible endogenous ligand(s) that may be natural activators for the disclosed orphan GPCRs.

B. Receptor Screening

Techniques have become more readily available over the past few years for

endogenous-ligand identification (this, primarily, for the purpose of providing a means of conducting receptor-binding assays that require a receptor's endogenous ligand) because the traditional study of receptors has always proceeded from the a priori assumption (historically based) that the endogenous ligand must first be identified before discovery could proceed to find antagonists and other molecules that could affect the receptor. Even in cases where an antagonist might have been known first, the search immediately extended to looking for the endogenous ligand. This mode of thinking has persisted in receptor research even after the discovery of constitutively activated receptors. What has not been heretofore recognized is that it is the active state of the receptor that is most useful for discovering agonists, partial agonists, and inverse agonists of the receptor. For those diseases which result from an overly active receptor or an under-active receptor, what is desired in a therapeutic drug is a compound which acts to diminish the active state of a receptor or enhance the activity of the receptor, respectively, not necessarily a drug which is an antagonist to the endogenous ligand. This is because a compound that reduces or enhances the activity of the active receptor state need not bind at the same site as the endogenous ligand. Thus, as taught by a method of this invention, any search for therapeutic compounds should start by screening compounds against the ligand-independent active state.

As is known in the art, GPCRs can be "active" in their endogenous state even without the binding of the receptor's endogenous ligand thereto. Such naturally-active receptors can be screened for the direct identification (*i.e.*, without the need for the receptor's endogenous ligand) of, in particular, inverse agonists. Alternatively, the receptor can be "activated" via, *e.g.*, mutation of the receptor to establish a non-endogenous version of the receptor that is active in the absence of the receptor's endogenous ligand.

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Screening candidate compounds against an endogenous or non-endogenous, constitutively activated version of the human orphan GPCRs disclosed herein can provide for the direct identification of candidate compounds which act at this cell surface receptor, without requiring use of the receptor's endogenous ligand. By determining areas within the body where the endogenous version of human GPCRs disclosed herein is expressed and/or over-expressed, it is possible to determine related disease/disorder states which are associated with the expression and/or over-expression of the receptor; such an approach is disclosed in this patent document.

With respect to creation of a mutation that may evidence constitutive activation of 10 human orphan GPCRs disclosed herein is based upon the distance from the proline residue at which is presumed to be located within TM6 of the GPCR typically nears the TM6/IC3 interface (such proline residue appears to be quite conserved). By mutating the amino acid residue located 16 amino acid residues from this residue (presumably located in the IC3 region of the receptor) to, most preferably, a lysine residue, such activation may be obtained. 15 Other amino acid residues may be useful in the mutation at this position to achieve this objective.

C. Disease/Disorder Identification and/or Selection

Preferably, the DNA sequence of the human orphan GPCR can be used to make a probe for (a) dot-blot analysis against tissue-mRNA, and/or (b) RT-PCR identification of 20 the expression of the receptor in tissue samples. The presence of a receptor in a tissue source, or a diseased tissue, or the presence of the receptor at elevated concentrations in diseased tissue compared to a normal tissue, can be preferably utilized to identify a correlation with a treatment regimen, including but not limited to, a disease associated

with that disease. Receptors can equally well be localized to regions of organs by this technique. Based on the known functions of the specific tissues to which the receptor is localized, the putative functional role of the receptor can be deduced.

D. Screening of Candidate Compounds

5 1. Generic GPCR screening assay techniques

When a G protein receptor becomes constitutively active (i.e., active in the absence of endogenous ligand binding thereto), it binds to a G protein (e.g., Gq, Gs, Gi, Go) and stimulates the binding of GTP to the G protein. The G protein then acts as a GTPase and slowly hydrolyzes the GTP to GDP, whereby the receptor, under normal conditions, becomes
10 deactivated. However, constitutively activated receptors continue to exchange GDP to GTP.

A non-hydrolyzable analog of GTP, [³⁵S]GTPγS, can be used to monitor enhanced binding to membranes which express constitutively activated receptors. It is reported that [³⁵S]GTPγS can be used to monitor G protein coupling to membranes in the absence and presence of ligand. An example of this monitoring, among other examples well-known and
15 available to those in the art, was reported by Traynor and Nahorski in 1995. The preferred use of this assay system is for initial screening of candidate compounds because the system is generically applicable to all G protein-coupled receptors regardless of the particular G protein that interacts with the intracellular domain of the receptor.

2. Specific GPCR screening assay techniques

20 Once candidate compounds are identified using the "generic" G protein-coupled receptor assay (i.e., an assay to select compounds that are agonists, partial agonists, or inverse agonists), further screening to confirm that the compounds have interacted at the receptor site is preferred. For example, a compound identified by the "generic" assay may not bind to the

receptor, but may instead merely "uncouple" the G protein from the intracellular domain.

a. Gs and Gi.

Gs stimulates the enzyme adenylyl cyclase. Gi (and Go), on the other hand, inhibit this enzyme. Adenylyl cyclase catalyzes the conversion of ATP to cAMP; thus, 5 constitutively activated GPCRs that couple the Gs protein are associated with increased cellular levels of cAMP. On the other hand, constitutively activated GPCRs that couple the Gi (or Go) protein are associated with decreased cellular levels of cAMP. *See, generally, "Indirect Mechanisms of Synaptic Transmission," Chpt. 8, From Neuron To Brain (3rd Ed.) Nichols, J.G. et al eds. Sinauer Associates, Inc. (1992).* Thus, assays that detect cAMP can 10 be utilized to determine if a candidate compound is, *e.g.*, an inverse agonist to the receptor (*i.e.*, such a compound would decrease the levels of cAMP). A variety of approaches known in the art for measuring cAMP can be utilized; a most preferred approach relies upon the use of anti-cAMP antibodies in an ELISA-based format. Another type of assay that can be utilized is a whole cell second messenger reporter system assay. Promoters on genes drive 15 the expression of the proteins that a particular gene encodes. Cyclic AMP drives gene expression by promoting the binding of a cAMP-responsive DNA binding protein or transcription factor (CREB) which then binds to the promoter at specific sites called cAMP response elements and drives the expression of the gene. Reporter systems can be constructed which have a promoter containing multiple cAMP response elements before the reporter 20 gene, *e.g.*, β -galactosidase or luciferase. Thus, a constitutively activated Gs-linked receptor causes the accumulation of cAMP that then activates the gene and expression of the reporter protein. The reporter protein such as β -galactosidase or luciferase can then be detected using standard biochemical assays (Chen et al. 1995).

Go and Gq.

Gq and Go are associated with activation of the enzyme phospholipase C, which in turn hydrolyzes the phospholipid PIP_2 , releasing two intracellular messengers: diacylglycerol (DAG) and inistol 1,4,5-triphoisphate (IP_3). Increased accumulation of IP_3 is associated with activation of Gq- and Go-associated receptors. *See, generally, "Indirect Mechanisms of Synaptic Transmission," Chpt. 8, From Neuron To Brain (3rd Ed.) Nichols, J.G. et al eds. Sinauer Associates, Inc. (1992).* Assays that detect IP_3 accumulation can be utilized to determine if a candidate compound is, *e.g.*, an inverse agonist to a Gq- or Go-associated receptor (*i.e.*, such a compound would decrease the levels of IP_3). Gq-associated receptors can also been examined using an AP1 reporter assay in that Gq-dependent phospholipase C causes activation of genes containing AP1 elements; thus, activated Gq-associated receptors will evidence an increase in the expression of such genes, whereby inverse agonists thereto will evidence a decrease in such expression, and agonists will evidence an increase in such expression. Commercially available assays for such detection are available.

3. GPCR Fusion Protein

The use of an endogenous, constitutively activated orphan GPCR, or a non-endogenous, constitutively activated orphan GPCR, for screening of candidate compounds for the direct identification of inverse agonists, agonists and partial agonists provides a unique challenge in that, by definition, the receptor is active even in the absence of an endogenous ligand bound thereto. Thus, it is often useful that an approach be utilized that can enhance the signal obtained by the activated receptor. A preferred approach is the use of a GPCR Fusion Protein.

Generally, once it is determined that a GPCR is or has been constitutively activated, using the assay techniques set forth above (as well as others), it is possible to determine the predominant G protein that couples with the endogenous GPCR. Coupling of the G protein to the GPCR provides a signaling pathway that can be assessed. Because it is most preferred that screening take place by use of a mammalian expression system, such a system will be expected to have endogenous G protein therein. Thus, by definition, in such a system, the constitutively activated orphan GPCR will continuously signal. In this regard, it is preferred that this signal be enhanced such that in the presence of, *e.g.*, an inverse agonist to the receptor, it is more likely that it will be able to more readily differentiate, particularly in the context of screening, between the receptor when it is contacted with the inverse agonist.

The GPCR Fusion Protein is intended to enhance the efficacy of G protein coupling with the GPCR. The GPCR Fusion Protein is preferred for screening with a non-endogenous, constitutively activated GPCR because such an approach increases the signal that is most preferably utilized in such screening techniques, although the GPCR Fusion Protein can also be (and preferably is) used with an endogenous, constitutively activated GPCR. This is important in facilitating a significant "signal to noise" ratio; such a significant ratio is important preferred for the screening of candidate compounds as disclosed herein.

The construction of a construct useful for expression of a GPCR Fusion Protein is within the purview of those having ordinary skill in the art. Commercially available expression vectors and systems offer a variety of approaches that can fit the particular needs of an investigator. The criteria of importance for such a GPCR Fusion Protein construct is that the GPCR sequence and the G protein sequence both be in-frame (preferably, the sequence for the GPCR is upstream of the G protein sequence) and that the "stop" codon of

the GPCR must be deleted or replaced such that upon expression of the GPCR, the G protein can also be expressed. The GPCR can be linked directly to the G protein, or there can be spacer residues between the two (preferably, no more than about 12, although this number can be readily ascertained by one of ordinary skill in the art). We have a preference (based upon convenience) of use of a spacer in that some restriction sites that are not used will, effectively, upon expression, become a spacer. Most preferably, the G protein that couples to the GPCR will have been identified prior to the creation of the GPCR Fusion Protein construct. Because there are only a few G proteins that have been identified, it is preferred that a construct comprising the sequence of the G protein (*i.e.*, a universal G protein construct) be available for insertion of an endogenous GPCR sequence therein; this provides for efficiency in the context of large-scale screening of a variety of different endogenous GPCRs having different sequences.

E. Other Utility

Although a preferred use of the human orphan GPCRs disclosed herein may be for the direct identification of candidate compounds as inverse agonists, agonists or partial agonists (preferably for use as pharmaceutical agents), these versions of human GPCRs can also be utilized in research settings. For example, *in vitro* and *in vivo* systems incorporating GPCRs can be utilized to further elucidate and understand the roles these receptors play in the human condition, both normal and diseased, as well as understanding the role of constitutive activation as it applies to understanding the signaling cascade. The value in human orphan GPCRs is that its utility as a research tool is enhanced in that by determining the location(s) of such receptors within the body, the GPCRs can be used to understand the role of these receptors in the human body before the endogenous ligand therefor is identified.

Other uses of the disclosed receptors will become apparent to those in the art based upon, *inter alia*, a review of this patent document.

EXAMPLES

The following examples are presented for purposes of elucidation, and not limitation, of the present invention. While specific nucleic acid and amino acid sequences are disclosed herein, those of ordinary skill in the art are credited with the ability to make minor modifications to these sequences while achieving the same or substantially similar results reported below. Unless otherwise indicated below, all nucleic acid sequences for the disclosed endogenous orphan human GPCRs have been sequenced and verified. For 10 purposes of equivalent receptors, those of ordinary skill in the art will readily appreciate that conservative substitutions can be made to the disclosed sequences to obtain a functionally equivalent receptor.

Example 1

ENDOGENOUS HUMAN GPCRS

15 1. Identification of Human GPCRs

Several of the disclosed endogenous human GPCRs were identified based upon a review of the GenBank database information. While searching the database, the following cDNA clones were identified as evidenced below.

| Disclosed | Accession | Complete DNA | Open Reading | Nucleic Acid | Amino |
|-----------|-----------|--------------|--------------|--------------|---------|
| 20 Human | Number | Sequence | Frame | SEQ.ID. | Acid |
| Orphan | | (Base Pairs) | (Base Pairs) | NO. | SEQ.ID. |
| GPCRs | | | | | NO. |

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| | | | | | | |
|---|---------------|----------|------------|----------|----|----|
| | hARE-3 | AL033379 | 111,389 bp | 1,260 bp | 1 | 2 |
| | hARE-4 | AC006087 | 226,925 bp | 1,119 bp | 3 | 4 |
| | hARE-5 | AC006255 | 127,605 bp | 1,104 bp | 5 | 6 |
| | hRUP3 | AL035423 | 140,094 bp | 1,005 bp | 7 | 8 |
| 5 | hRUP5 | AC005849 | 169,144 bp | 1,413 bp | 9 | 10 |
| | hRUP6 | AC005871 | 218,807 bp | 1,245 bp | 11 | 12 |
| | hRUP7 | AC007922 | 158,858 bp | 1,173 bp | 13 | 14 |

Other disclosed endogenous human GPCRs were identified by conducting a BLAST search of EST database (dbest) using the following EST clones as query sequences. The 10 following EST clones identified were then used as a probe to screen a human genomic library.

| | Disclosed | Query | EST Clone/ Accession No. | Open Reading Frame | Nucleic Acid SEQ.ID.NO. | Amino Acid SEQ.ID.NO. |
|----|----------------------------|----------------|------------------------------|--------------------------|----------------------------|--------------------------|
| | Human | (Sequence) | Identified | (Base Pairs) | | |
| 15 | Orphan GPCRs hGPCR27 | Mouse | AA775870 | 1,125 bp | 15 | 16 |
| | | GPCR27 TDAG | 1689643 | 999 bp | 17 | 18 |
| | | | AI090920 68530 | 1,122 bp | 19 | 20 |
| | | | AA359504 238667 | 1,053 bp | 21 | 22 |
| | | PPR1 | H67224 | | | |
| 20 | hG2A | Mouse | See Example 2(a), 1179426 | 1,113 bp | 23 | 24 |
| | | | below | | | |

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| | | | | | | |
|---|--------|--------------------------|-----------------------------|----------|----|----|
| | hCHN3 | N.A. | EST 36581 | 1,113 bp | 25 | 26 |
| | hCHN4 | TDAG | (full length) 1184934 | 1,077 bp | 27 | 28 |
| | hCHN6 | N.A. | AA804531 EST 2134670 | 1,503 bp | 29 | 30 |
| | hCHN8 | K1AA0001 | (full length) EST 764455 | 1,029 bp | 31 | 32 |
| 5 | hCHN 9 | 1365839 | EST 1541536 | 1,077 bp | 33 | 34 |
| | hCHN10 | Mouse EST | Human 1365839 | 1,005 bp | 35 | 36 |
| | hRUP4 | 1365839 N.A. | AI307658 | 1,296 bp | 37 | 38 |
| | | N.A. = "not applicable". | | | | |

2. Full Length Cloning

10 a. hG2A (Seq. Id. Nos. 23 & 24)

Mouse EST clone 1179426 was used to obtain a human genomic clone containing all but three amino acid hG2A coding sequences. The 5' end of this coding sequence was obtained by using 5'RACE™, and the template for PCR was Clontech's Human Spleen Marathon-ready™ cDNA. The disclosed human G2A was amplified by PCR using the G2A
15 cDNA specific primers for the first and second round PCR as shown in SEQ.ID.NO.: 39 and SEQ.ID.NO.:40 as follows:

5'-CTGTGTACAGCAGTTCGCAGAGTG-3' (SEQ.ID.NO.: 39; 1st round PCR)

5'-GAGTGCCAGGCAGAGCAGGTAGAC-3' (SEQ.ID.NO.: 40; second round PCR).

PCR was performed using Advantage™ GC Polymerase Kit (Clontech; manufacturing
20 instructions will be followed), at 94°C for 30 sec followed by 5 cycles of 94°C for 5 sec and 72°C for 4 min; and 30 cycles of 94° for 5 sec and 70° for 4 min. An approximate 1.3 Kb PCR fragment was purified from agarose gel, digested with Hind III and Xba I and cloned into the expression vector pRC/CMV2 (Invitrogen). The cloned-insert was sequenced using the T7 Sequenase™ kit (USB Amersham; manufacturer instructions will be followed) and

the sequence was compared with the presented sequence. Expression of the human G2A will be detected by probing an RNA dot blot (Clontech; manufacturer instructions will be followed) with the P³²-labeled fragment.

b. hCHN9 (Seq. Id. Nos. 33 & 34)

5 Sequencing of the EST clone 1541536 indicated that hCHN9 is a partial cDNA clone having only an initiation codon; *i.e.*, the termination codon was missing. When hCHN9 was used to "blast" against the data base (nr), the 3' sequence of hCHN9 was 100% homologous to the 5' untranslated region of the leukotriene B4 receptor cDNA, which contained a termination codon in the frame with hCHN9 coding sequence. To
10 determine whether the 5' untranslated region of LTB4R cDNA was the 3' sequence of hCHN9, PCR was performed using primers based upon the 5' sequence flanking the initiation codon found in hCHN9 and the 3' sequence around the termination codon found in the LTB4R 5' untranslated region. The 5' primer sequence utilized was as follows:

5'-CCCGAATTCCTGCTTGCTCCCAGCTTGGCCC-3' (SEQ.ID.NO.: 41; sense) and

15 5'-TGTGGATCCTGCTGTCAAAGGTCCCATTCGGG-3' (SEQ.ID.NO.: 42; antisense).

PCR was performed using thymus cDNA as a template and rTth polymerase (Perkin Elmer) with the buffer system provided by the manufacturer, 0.25 uM of each primer, and 0.2 mM of each 4 nucleotides. The cycle condition was 30 cycles of 94°C for 1 min, 65°C for 1min
of each 4 nucleotides. The cycle condition was 30 cycles of 94°C for 1 min, 65°C for 1min and 72 °C for 1 min and 10 sec. A 1.1kb fragment consistent with the predicted size was
20 obtained from PCR. This PCR fragment was subcloned into pCMV (*see below*) and sequenced (*see*, SEQ.ID.NO.: 33).

c. hRUP 4 (Seq. Id. Nos. 37 & 38)

The full length hRUP4 was cloned by RT-PCR with human brain cDNA (Clontech)

as templates:

5'-TCACAATGCTAGGTGTGGTC-3' (SEQ.ID.NO.: 43; sense) and

5'-TGCATAGACAATGGGATTACAG-3' (SEQ.ID.NO.: 44; antisense).

PCR was performed using TaqPlus™ Precision™ polymerase (Stratagene; manufacturing instructions will be followed) by the following cycles: 94°C for 2 min; 94°C 30 sec; 55°C for 30 sec, 72°C for 45 sec, and 72°C for 10 min. Cycles 2 through 4 were repeated 30 times.

The PCR products were separated on a 1% agarose gel and a 500 bp PCR fragment was isolated and cloned into the pCRII-TOPO vector (Invitrogen) and sequenced using the T7 DNA Sequenase™ kit (Amsham) and the SP6/T7 primers (Stratagene). Sequence analysis revealed that the PCR fragment was indeed an alternatively spliced form of AI307658 having a continuous open reading frame with similarity to other GPCRs. The completed sequence of this PCR fragment was as follows:

5'-TCACAATGCTAGGTGTGGTCTGGCTGGTGGCAGTCATCGTAGGATCACCCATGTGGCAC
 15 GTGCAACAACCTGAGATCAAAATGACTTCCTATATGAAAAGGAACACATCTGCTGCTTAGAA
 GAGTGGACCAGCCCTGTGCACCAGAAGATCTACACCACCTTCATCCTTGTCATCCTCTTCCTCC
 TGCCTCTTATGGTGATGCTTATTCTGTACGTAATAATGGTTATGAACCTTTGGATAAAAGAAAAGA
 GTTGGGGATGGTTCAGTGCTTCGAACTATTCATGGAAAAAGAAATGTCCAAAATAGCCAGGAAG
 AAGAAACGAGCTGTCATTATGATGGTGACAGTGGTGGCTCTCTTTGCTGTGTGCTGGGCACCA
 20 TTCCATGTTGTCCATATGATGATTGAATACAGTAATTTTGAAAAGGAATATGATGATGTCACA
 ATCAAGATGATTTTGCTATCGTGCAAATATTTGGATTTTCCAACCTCCATCTGTAATCCCATTTG
 TCTATGCA-3' (SEQ.ID.NO.: 45)

Based on the above sequence, two sense oligonucleotide primer sets:

5'-CTGCTTAGAAGAGTGGACCAG-3' (SEQ.ID.NO.: 46; oligo 1),

25 5'-CTGTGCACCAGAAGATCTACAC-3' (SEQ.ID.NO.: 47; oligo 2)

and two antisense oligonucleotide primer sets:

5'-CAAGGATGAAGGTGGTGTAGA-3' (SEQ.ID.NO.: 48; oligo 3)

5'-GTGTAGATCTTCTGGTGCACAGG-3' (SEQ.ID.NO.: 49; oligo 4)

were used for 3'- and 5'-race PCR with a human brain Marathon-Ready™ cDNA (Clontech,

Cat# 7400-1) as template, according to manufacture's instructions. DNA fragments generated by the RACE PCR were cloned into the pCRII-TOPO™ vector (Invitrogen) and sequenced using the SP6/T7 primers (Stratagene) and some internal primers. The 3' RACE product contained a poly(A) tail and a completed open reading frame ending at a TAA stop codon. The 5' RACE product contained an incomplete 5' end; *i.e.*, the ATG initiation codon was not present.

Based on the new 5' sequence, oligo 3 and the following primer:

5'-GCAATGCAGGTCATAGTGAGC-3' (SEQ.ID.NO.: 50; oligo 5)

were used for the second round of 5' RACE PCR and the PCR products were analyzed as 10 above. A third round of 5' RACE PCR was carried out utilizing antisense primers:

5'-TGGAGCATGGTGACGGGAATGCAGAAG-3' (SEQ.ID.NO.: 51; oligo 6) and

5'-GTGATGAGCAGGTCAGTACGCGCAAG-3' (SEQ.ID.NO.: 52; oligo 7).

The sequence of the 5' RACE PCR products revealed the presence of the initiation codon ATG, and further round of 5' RACE PCR did not generate any more 5' sequence. The 15 completed 5' sequence was confirmed by RT-PCR using sense primer

5'-GCAATGCAGGCGCTTAACATTAC-3' (SEQ.ID.NO.: 53; oligo 8)

and oligo 4 as primers and sequence analysis of the 650 bp PCR product generated from human brain and heart cDNA templates (Clontech, Cat# 7404-1). The completed 3' sequence was confirmed by RT-PCR using oligo 2 and the following antisense primer:

20 5'-TTGGGTTACAATCTGAAGGGCA-3' (SEQ.ID.NO.: 54; oligo 9)

and sequence analysis of the 670 bp PCR product generated from human brain and heart cDNA templates. (Clontech, Cat# 7404-1).

d. hRUP5 (Seq. Id. Nos. 9 & 10)

The full length hRUP5 was cloned by RT-PCR using a sense primer upstream from

ATG, the initiation codon (SEQ.ID.NO.: 55), and an antisense primer containing TCA as the stop codon (SEQ.ID.NO.: 56), which had the following sequences:

5'-ACTCCGTGTCCAGCAGGACTCTG-3' (SEQ.ID.NO.:55)

5'-TGCGTGTTCCTGGACCCTCACGTG-3' (SEQ.ID.NO.: 56)

5 and human peripheral leukocyte cDNA (Clontech) as a template. Advantage cDNA polymerase (Clontech) was used for the amplification in a 50ul reaction by the following cycle with step 2 through step 4 repeated 30 times: 94°C for 30 sec; 94° for 15 sec; 69° for 40 sec; 72°C for 3 min; and 72°C for 6 min. A 1.4kb PCR fragment was isolated and cloned with the pCRII-TOPO™ vector (Invitrogen) and completely sequenced using the T7 DNA
10 Sequenase™ kit (Amsham). *See*, SEQ.ID.NO.: 9.

e. hRUP6 (Seq. Id. Nos. 11 & 12)

The full length hRUP6 was cloned by RT-PCR using primers:

5'-CAGGCCTTGGATTTTAATGTCAGGGATGG-3' (SEQ.ID.NO.: 57) and

5'-GGAGAGTCAGCTCTGAAAGAATTCAGG-3' (SEQ.ID.NO.: 58);

15 and human thymus Marathon-Ready™ cDNA (Clontech) as a template. Advantage cDNA polymerase (Clontech, according to manufacturer's instructions) was used for the amplification in a 50ul reaction by the following cycle: 94°C for 30sec; 94°C for 5 sec; 66°C for 40sec; 72°C for 2.5 sec and 72°C for 7 min. Cycles 2 through 4 were repeated 30 times. A 1.3 Kb PCR fragment was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen)
20 and completely sequenced (*see*, SEQ.ID.NO.: 11) using the ABI Big Dye Terminator™ kit (P.E. Biosystem).

f. hRUP7 (Seq. Id. Nos. 13 & 14)

The full length RUP7 was cloned by RT-PCR using primers:

5'-TGATGTGATGCCAGATACTAATAGCAC-3' (SEQ.ID.NO.: 59; sense) and

5'-CCTGATTCATTAGGTGAGATTGAGAC-3' (SEQ.ID.NO.: 60; antisense) and human peripheral leukocyte cDNA (Clontech) as a template. Advantage™ cDNA polymerase (Clontech) was used for the amplification in a 50 ul reaction by the following cycle with step 2 to step 4 repeated 30 times: 94°C for 2 minutes; 94°C for 15 seconds; 60°C for 20 seconds; 72°C for 2 minutes; 72°C for 10 minutes. A 1.25 Kb PCR fragment was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced using the ABI Big Dye Terminator™ kit (P.E. Biosystem). See, SEQ.ID.NO.: 13.

g. hARE-5 (Seq. Id. Nos. 5 & 6)

The full length hARE-5 was cloned by PCR using the hARE5 specific primers 10 5'-CAGCGCAGGGTGAAGCCTGAGAGC-3' SEQ.ID.NO.: 69 (sense, 5' of initiation codon ATG) and 5'-GGCACCTGCTGTGACCTGTGCAGG-3' SEQ.ID.NO.:70 (antisense, 3' of stop codon TGA) and human genomic DNA as template. TaqPlus Precision™ DNA polymerase (Stratagene) was used for the amplification by the following cycle with step 2 to step 4 repeated 35 times: 96°C, 2 minutes; 96°C, 20 seconds; 58°C, 30 seconds; 72°C, 2 minutes; and 72°C, 10 minutes

15 A 1.1 Kb PCR fragment of predicated size was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced (SEQ.ID.NO.:5) using the T7 DNA Sequenase™ kit (Amsham).

h. hARE-4 (Seq. Id. Nos.: 3 & 4)

The full length hARE-4 was cloned by PCR using the hARE-4 specific primers 5'-20 CTGGTGTGCTCCATGGCATCCC-3' SEQ.ID.NO.:67 (sense, 5' of initiation codon ATG) and 5'-GTAAGCCTCCCAGAACGAGAGG-3' SEQ.ID.NO.: 68 (antisense, 3' of stop codon TGA) and human genomic DNA as template. Taq DNA polymerase (Stratagene) and 5% DMSO was used for the amplification by the following cycle with step 2 to step 3 repeated 35 times:

94°C, 3 minutes; 94°C, 30 seconds; 59°C, 2 minutes; 72°C, 10 minutes

A 1.12 Kb PCR fragment of predicated size was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced (SEQ.ID.NO.:3) using the T7 DNA Sequenase™ kit (Amsham).

5 i. hARE-3 (Seq.Id.Nos.: 1 & 2)

The full length hARE-3 was cloned by PCR using the hARE-3 specific primers 5'-gatcaagcttCCATCCTACTGAAACCATGGTC-3' SEQ.ID.NO.:65 (sense, lower case nucleotides represent Hind III overhang, ATG as initiation codon) and 5'-gatcagatctCAGTTCCAATATTACACCAACCGTC-3' SEQ.ID.NO.:66 (antisense, lower case 10 nucleotides represent Xba I overhang, TCA as stop codon) and human genomic DNA as template. TaqPlus Precision™ DNA polymerase (Stratagene) was used for the amplification by the following cycle with step 2 to step 4 repeated 35 times: 94°C, 3 minutes; 94°C, 1 minute; 55°C, 1 minute; 72°C, 2 minutes; 72°C, 10 minutes.

A 1.3 Kb PCR fragment of predicated size was isolated and digested with Hind III 15 and Xba I, cloned into the pRC/CMV2 vector (Invitrogen) at the Hind III and Xba I sites and completely sequenced (SEQ.ID.NO.:1) using the T7 DNA Sequenase™ kit (Amsham).

 j. hRUP3 (Seq. Id. Nos.:7 & 8)

The full length hRUP3 was cloned by PCR using the hRUP3 specific primers 5'-GTCCTGCCACTTCGAGACATGG-3' SEQ.ID.NO.:71 (sense, ATG as initiation codon) and 5'-20 GAAACTTCTCTGCCCTTACCGTC-3' SEQ.ID.NO.:72 (antisense, 3' of stop codon TAA) and human genomic DNA as template. TaqPlus Precision™ DNA polymerase (Stratagene) was used for the amplification by the following cycle with step 2 to step 4 repeated 35 times: 94°C, 3 minutes; 94°C, 1 minute; 58°C, 1 minute; 72°C, 2 minutes; 72°C, 10 minutes

A 1.0 Kb PCR fragment of predicated size was isolated and cloned into the pCRII-TOPO™ vector (Invitrogen) and completely sequenced (SEQ.ID.NO.: 7) using the T7 DNA sequenase kit (Amsham).

Example 2

5 RECEPTOR EXPRESSION

Although a variety of cells are available to the art for the expression of proteins, it is most preferred that mammalian cells be utilized. The primary reason for this is predicated upon practicalities, *i.e.*, utilization of, *e.g.*, yeast cells for the expression of a GPCR, while possible, introduces into the protocol a non-mammalian cell which may not (indeed, in the 10 case of yeast, does not) include the receptor-coupling, genetic-mechanism and secretory pathways that have evolved for mammalian systems - thus, results obtained in non-mammalian cells, while of potential use, are not as preferred as that obtained from mammalian cells. Of the mammalian cells, COS-7, 293 and 293T cells are particularly preferred, although the specific mammalian cell utilized can be predicated upon the particular 15 needs of the artisan. The general procedure for expression of the disclosed GPCRs is as follows.

On day one, 1×10^7 293T cells per 150mm plate were plated out. On day two, two reaction tubes will be prepared (the proportions to follow for each tube are per plate): tube A will be prepared by mixing 20 μ g DNA (*e.g.*, pCMV vector; pCMV vector with receptor 20 cDNA, etc.) in 1.2ml serum free DMEM (Irvine Scientific, Irvine, CA); tube B will be prepared by mixing 120 μ l lipofectamine (Gibco BRL) in 1.2ml serum free DMEM. Tubes A and B are admixed by inversions (several times), followed by incubation at room temperature for 30-45min. The admixture can be referred to as the "transfection mixture". Plated 293T cells are washed with 1XPBS, followed by addition of 10ml serum free DMEM.

2.4ml of the transfection mixture will then be added to the cells, followed by incubation for 4hrs at 37°C/5% CO₂. The transfection mixture was then be removed by aspiration, followed by the addition of 25ml of DMEM/10% Fetal Bovine Serum. Cells will then be incubated at 37°C/5% CO₂. After 72hr incubation, cells can then be harvested and utilized for analysis.

5 Example 3

TISSUE DISTRIBUTION OF THE DISCLOSED HUMAN GPCRS

Several approaches can be used for determination of the tissue distribution of the GPCRs disclosed herein.

1. Dot-Blot Analysis

10 Using a commercially available human-tissue dot-blot format, endogenous orphan GPCRs were probed for a determination of the areas where such receptors are localized. cDNA fragments from the GPCRs of Example 1 (radiolabelled) were (or can be) used as the probe: radiolabeled probe was (or can be) generated using the complete receptor cDNA (excised from the vector) using a Prime-It II™ Random Primer Labeling Kit (Stratagene, 15 #300385), according to manufacturer's instructions. A human RNA Master Blot™ (Clontech, #7770-1) was hybridized with the endogenous human GPCR radiolabeled probe and washed under stringent conditions according manufacturer's instructions. The blot was exposed to Kodak BioMax™ Autoradiography film overnight at -80°C. Results are summarized for several receptors in Table B and C (see Figures 1A and 1B for a grid 20 identifying the various tissues and their locations, respectively). Exemplary dot-blots are provided in Figure 2A and 2B for results derived using hCHN3 and hCHN8, respectively.

TABLE B

ORPHAN GPCR

Tissue Distribution
(highest levels, relative to other tissues in the dot-blot)

- 27 -

| | | |
|---|---------|--|
| | hGPCR27 | Fetal brain, Putamen, Pituitary gland, Caudate nucleus |
| | hARE-1 | Spleen, Peripheral leukocytes, Fetal spleen |
| | hPPR1 | Pituitary gland, Heart, salivary gland, Small intestine, Testis- |
| | hRUP3 | Pancreas |
| 5 | hCHN3 | Fetal brain, Putamen, Occipital cortex |
| | hCHN9 | Pancreas, Small intestine, Liver |
| | hCHN10 | Kidney, Thryoid |

TABLE C

| | ORPHAN GPCR | Tissue Distribution (highest levels, relative to other tissues in the dot-blot) |
|----|-------------|--|
| 10 | hARE-3 | Cerebellum left, Cerebellum right, Testis, Accumbens |
| | hGPCR3 | Corpus collusum, Caudate nucleus, Liver, Heart, Inter-Ventricular Septum |
| | hARE-2 | Cerebellum left, Cerebellum right, Substantia |
| | hCHN8 | Cerebellum left, Cerebellum right, Kidney, Lung |

2. RT-PCR

15 a. hRUP3

To ascertain the tissue distribution of hRUP3 mRNA, RT-PCR was performed using hRUP3-specific primers and human multiple tissue cDNA panels (MTC, Clontech) as templates. Taq DNA polymerase (Stratagene) was utilized for the PCR reaction, using the following reaction cycles in a 40ul reaction: 94°C for 2 min; 94°C for 15 sec; 55°C for 30 sec; 72°C for 1 min; 72°C, for 10 min. Primers were as follows:

5'-GACAGGTACCTTGCCATCAAG-3' (SEQ.ID.NO.: 61; sense)

5'-CTGCACAATGCCAGTGATAAGG-3' (SEQ.ID.NO.: 62; antisense).

20ul of the reaction was loaded onto a 1% agarose gel; results are set forth in Figure 3.

As is supported by the data of Figure 3, of the 16 human tissues in the cDNA panel utilized (brain, colon, heart, kidney, lung, ovary, pancreas, placenta, prostate, skeleton, small intestine, spleen, testis, thymus leukocyte, and liver) a single hRUP3 band is evident only from the pancreas. Additional comparative analysis of the protein sequence of hRUP3 with 5 other GPCRs suggest that hRUP3 is related to GPCRs having small molecule endogenous ligand such that it is predicted that the endogenous ligand for hRUP3 is a small molecule.

b. hRUP4

RT-PCR was performed using hRUP4 oligo's 8 and 4 as primers and the human multiple tissue cDNA panels (MTC, Clontech) as templates. Taq DNA polymerase 10 (Stratagene) was used for the amplification in a 40ul reaction by the following cycles: 94°C for 30 seconds, 94°C for 10 seconds, 55°C for 30 seconds, 72°C for 2 minutes, and 72°C for 5 minutes with cycles 2 through 4 repeated 30 times.

20 μ l of the reaction were loaded on a 1% agarose gel to analyze the RT-PCR products, and hRUP4 mRNA was found expressed in many human tissues, with the strongest 15 expression in heart and kidney. (see, Figure 4). To confirm the authenticity of the PCR fragments, a 300 bp fragment derived from the 5' end of hRUP4 was used as a probe for the Southern Blot analysis. The probe was labeled with 32 P-dCTP using the Prime-It II™ Random Primer Labeling Kit (Stratagene) and purified using the ProbeQuant™ G-50 micro columns (Amersham). Hybridization was done overnight at 42° C following a 12 hr pre- 20 hybridization. The blot was finally washed at 65°C with 0.1 x SSC. The Southern blot did confirm the PCR fragments as hRUP4.

c. hRUP5

RT-PCR was performed using the following hRUP5 specific primers:

5'-CTGACTTCTGTTCCTGGCAGCAGCGG-3' (SEQ.ID.NO.: 63; sense)

5'-AGACCAGCCAGGGCACGCTGAAGAGTG-3' (SEQ.ID.NO.: 64; antisense)

and the human multiple tissue cDNA panels (MTC, Clontech) as templates. Taq DNA polymerase (Stratagene) was used for the amplification in a 40ul reaction by the following cycles: 94°C for 30 sec, 94°C for 10 sec, 62°C for 1.5 min, 72°C for 5 min, and with cycles 2 through 3 repeated 30 times. 20 µl of the reaction were loaded on a 1.5% agarose gel to analyze the RT-PCR products, and hRUP5 mRNA was found expressed only in the peripheral blood leukocytes (*data not shown*).

10 **d. hRUP6**

RT-PCR was applied to confirm the expression and to determine the tissue distribution of hRUP6. Oligonucleotides used, based on an alignment of AC005871 and GPR66 segments, had the following sequences:

5'-CCAACACCAGCATCCATGGCATCAAG-3' (SEQ.ID.NO.: 73; sense),

15 5'-GGAGAGTCAGCTCTGAAAGAATTCAGG-3' (SEQ.ID.NO.: 74; antisense)

and the human multiple tissue cDNA panels (MTC, Clontech) were used as templates.

PCR was performed using TaqPlus Precision™ polymerase (Stratagene; manufacturing instructions will be followed) in a 40ul reaction by the following cycles: 94°C for 30 sec; 94°C 5 sec; 66°C for 40 sec, 72°C for 2.5 min, and 72°C for 7 min. Cycles 2 through 4 20 were repeated 30 times.

20 ul of the reaction were loaded on a 1.2% agarose gel to analyze the RT-PCR products, and a specific 760bp DNA fragment representing hRUP6 was expressed predominantly in the thymus and with less expression in the heart, kidney, lung, prostate small intestine and testis. (*see, Figure 5*).

It is intended that each of the patents, applications, and printed publications mentioned in this patent document be hereby incorporated by reference in their entirety.

As those skilled in the art will appreciate, numerous changes and modifications may be made to the preferred embodiments of the invention without departing from the spirit of the invention. It is intended that all such variations fall within the scope of the invention and the claims that follow.

Although a variety of Vectors are available to those in the art, for purposes of utilization for both endogenous and non-endogenous human GPCRs, it is most preferred that the Vector utilized be pCMV. This vector was deposited with the American Type Culture Collection (ATCC) on October 13, 1998 (10801 University Blvd., Manassas, VA 20110-2209 USA) under the provisions of the Budapest Treaty for the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure. The DNA was tested by the ATCC and determined to be. The ATCC has assigned the following deposit number to pCMV: ATCC #203351.

CLAIMS

What is claimed is:

1. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 1.
- 5 2. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 1 comprising SEQ.ID.NO.: 2.
3. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:1.
4. A Host Cell comprising the Plasmid of claim 3.
5. A cDNA encoding a human G protein-coupled receptor comprising
10 SEQ.ID.NO.: 3.
6. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 3 comprising SEQ.ID.NO.: 4.
7. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:3.
8. A Host Cell comprising the Plasmid of claim 7.
- 15 9. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 5.
10. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 5 comprising SEQ.ID.NO.: 6.
11. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:5.
- 20 12. A Host Cell comprising the Plasmid of claim 11.
13. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 7.

14. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 7 comprising SEQ.ID.NO.: 8.
15. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:7.
16. A Host Cell comprising the Plasmid of claim 15.
- 5 17. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 9.
18. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 9 comprising SEQ.ID.NO.: 10.
19. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:9.
- 10 20. A Host Cell comprising the Plasmid of claim 19.
21. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 11.
22. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 11 comprising SEQ.ID.NO.:12.
- 15 23. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:11.
24. A Host Cell comprising the Plasmid of claim 23.
25. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 13.
26. A human G protein-coupled receptor encoded by the cDNA of
20 SEQ.ID.NO.: 13 comprising SEQ.ID.NO.: 14.
27. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:13.
28. A Host Cell comprising the Plasmid of claim 27.
29. A cDNA encoding a human G protein-coupled receptor comprising

SEQ.ID.NO.: 15.

30. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 15 comprising SEQ.ID.NO.: 16.

31. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:15.

5 32. A Host Cell comprising the Plasmid of claim 31.

33. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 17.

34. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 17 comprising SEQ.ID.NO.: 18.

10 35. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:17.

36. A Host Cell comprising the Plasmid of claim 35.

37. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 19.

38. A human G protein-coupled receptor encoded by the cDNA of
15 SEQ.ID.NO.: 19 comprising SEQ.ID.NO.: 20.

39. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:19.

40. A Host Cell comprising the Plasmid of claim 39.

41. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 21.

20 42. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 21 comprising SEQ.ID.NO.: 22.

43. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:21.

44. A Host Cell comprising the Plasmid of claim 43.

45. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 23.
46. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 23 comprising SEQ.ID.NO.: 24.
- 5 47. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.: 23.
48. A Host Cell comprising the Plasmid of claim 47.
49. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 25.
50. A human G protein-coupled receptor encoded by the cDNA of
10 SEQ.ID.NO.: 25 comprising SEQ.ID.NO.: 26.
51. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.: 25.
52. A Host Cell comprising the Plasmid of claim 51.
53. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 27.
- 15 54. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 27 comprising SEQ.ID.NO.: 28.
55. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.: 27.
56. A Host Cell comprising the Plasmid of claim 55.
57. A cDNA encoding a human G protein-coupled receptor comprising
20 SEQ.ID.NO.: 29.
58. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 29 comprising SEQ.ID.NO.: 30.
59. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.: 29.

60. A Host Cell comprising the Plasmid of claim 59.
61. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 31.
62. A human G protein-coupled receptor encoded by the cDNA of
5 SEQ.ID.NO.: 31 comprising SEQ.ID.NO.: 32.
63. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:31.
64. A Host Cell comprising the Plasmid of claim 63.
65. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 33.
- 10 66. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 33 comprising SEQ.ID.NO.: 34.
67. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:33.
68. A Host Cell comprising the Plasmid of claim 67.
69. A cDNA encoding a human G protein-coupled receptor comprising
15 SEQ.ID.NO.: 35.
70. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 35 comprising SEQ.ID.NO.: 36.
71. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:35.
72. A Host Cell comprising the Plasmid of claim 71.
- 20 73. A cDNA encoding a human G protein-coupled receptor comprising
SEQ.ID.NO.: 37.
74. A human G protein-coupled receptor encoded by the cDNA of
SEQ.ID.NO.: 37 comprising SEQ.ID.NO.: 38.

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75. A Plasmid comprising a Vector and the cDNA of SEQ.ID.NO.:37.
76. A Host Cell comprising the Plasmid of claim 75.

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|---|------------------|-------------|------------------|-----------------|-----------------|----------------------|----------------|-------------------|
| A | | Amygdala | Caudate Nucleus | Cerebellum | Cerebral Cortex | Frontal Cortex | Hippocampus | Medulla Oblongata |
| B | Occipital Cortex | Putamen | Substantia Nigra | Temporal Cortex | Thalamus | Accumbens | Spinal Cord | |
| C | Heart | Aorta | Skeletal Muscle | Colon | Bladder | Uterus | Prostate | Stomach |
| D | Testis | Ovary | Pancreas | Pituitary | Adrenal Gland | Thyroid | Salivary Gland | Mammary Gland |
| E | Kidney | Liver | Small Intestine | Spleen | Thymus | Peripheral Leukocyte | Lymph Node | Bone Marrow |
| F | Appendix | Lung | Trachea | Placenta | | | | |
| G | Fetal Brain | Fetal Heart | Fetal Kidney | Fetal Liver | Fetal Spleen | Fetal Thymus | Fetal Lung | |
| H | | | | | | | | |

FIG. 1A

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|----------------------|---------------------|--------------------------------|--------------------|---------------------|-------------------------|----------|-------------------|---------------------------------------|-----------------|----|
| A | | Cerebellum Left | Substantia Nigra | Heart | Esophagus | Colon Transverse | Kidney | Lung | Liver | Leukemia HL-60 | Fetal Brain | |
| B | Cerebral Cortex | Cerebellum Right | Accumbens | Aorta | Stomach | Colon Descending | Skeletal Muscle | Placenta | Pancreas | HeLa S3 | Fetal Heart | |
| C | Frontal Cortex | Corpus Callosum | Thalamus | Atrium Left | Duodenum | Rectum | Spleen | Bladder | Adrenal Gland | Leukemia K562 | Fetal Kidney | |
| D | Parietal Lobe | Amygdala | Pituitary Gland | Atrium Right | Jejunum | | Thymus | Uterus | Thyroid | Leukemia MOLT-4 | Fetal Liver | |
| E | Occipital Cortex | Caudate Nucleus | Spinal Cord | Ventricle Left | Ileum | | Peripheral Leukocyte | Prostate | Salivary Gland | Burkitt's Lymphoma Raji | Fetal Spleen | |
| F | Temporal Cortex | Hippocampus | | Ventricle Right | Ileocecum | | Lymph Node | Testis | Mammary Gland | Burkitt's Lymphoma Daudi | Fetal Thymus | |
| G | Paracentral Gyrus of Cerebral Cortex | Medulla Oblongata | | Inter Ventricular Septum | Appendix | | Bone Marrow | Ovary | | Colorectal Adenocarcinoma SW480 | Fetal Lung | |
| H | Pons | Putamen | | Apex of the Heart | Colon Ascending | | Trachea | | | Lung Carcinoma A549 | | |

FIG. 1B

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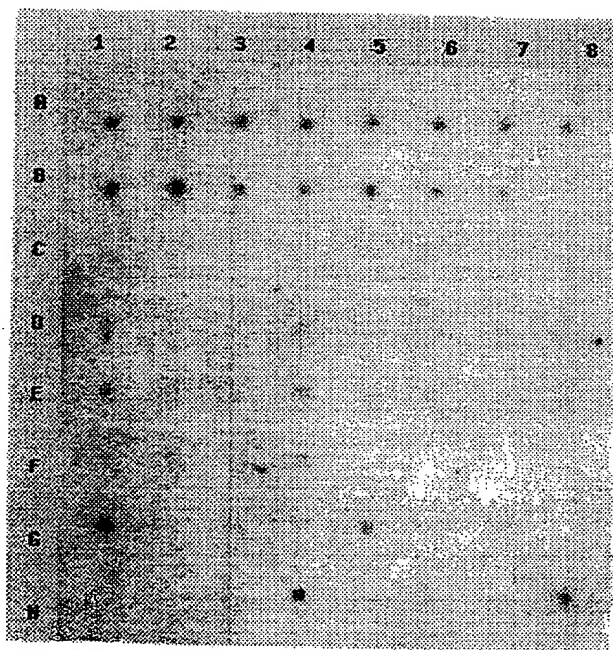


FIG. 2A

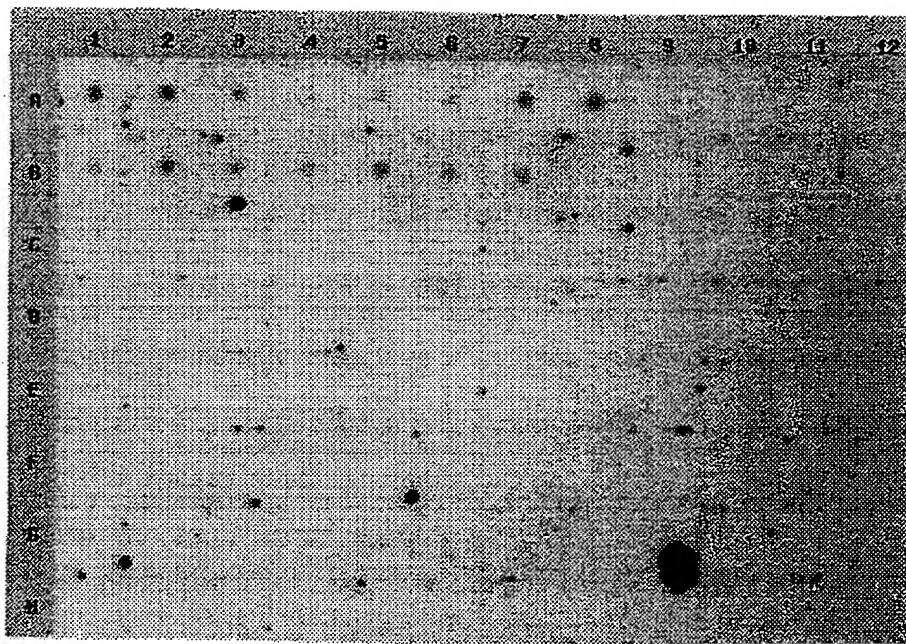


FIG. 2B

FIG. 5

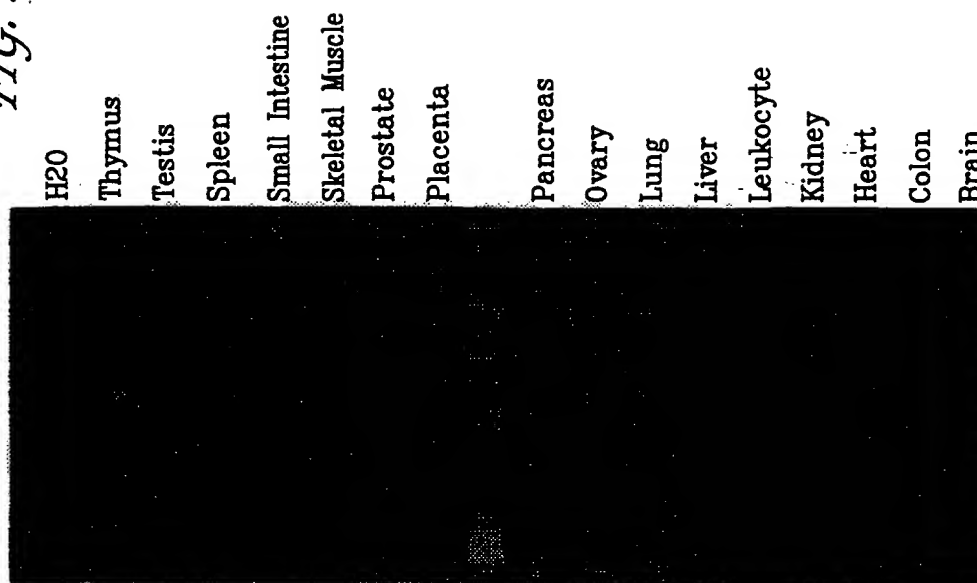


FIG. 4

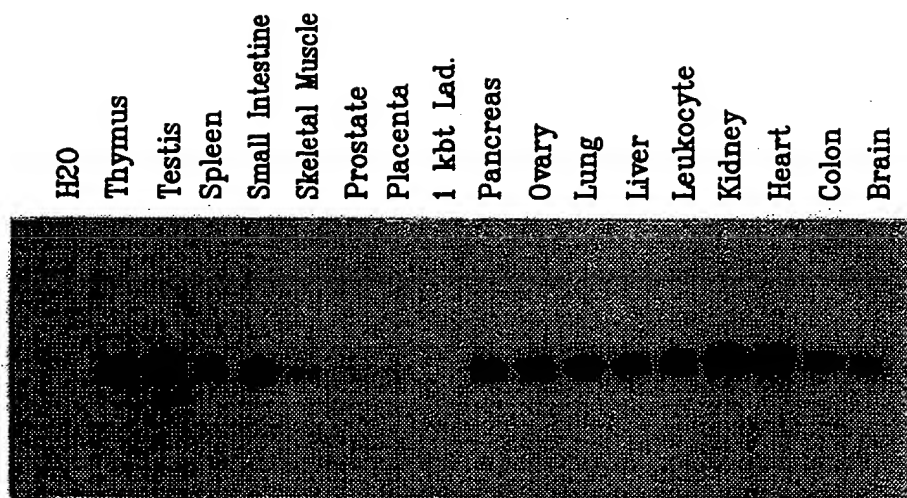
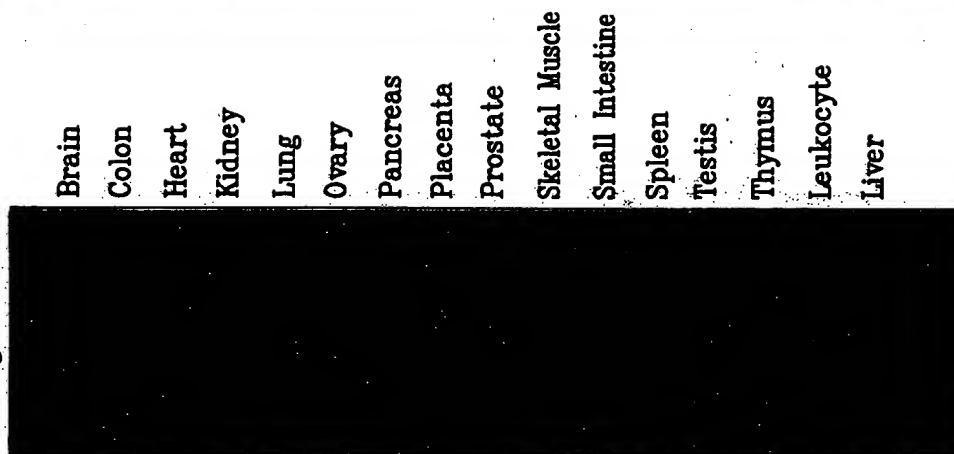


FIG. 3



- 1 -

SEQUENCE LISTING

(1) GENERAL INFORMATION:

- (i) APPLICANT: Chen, Ruoping
Dang, Huong T.
5 Liaw, Chen W.
Lin, I-Lin
- (ii) TITLE OF INVENTION: Human Orphan G Protein-Coupled Receptors
- (iii) NUMBER OF SEQUENCES: 74
- 10 (iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Arena Pharmaceuticals, Inc.
(B) STREET: 6166 Nancy Ridge Drive
(C) CITY: San Diego
(D) STATE: CA
15 (E) COUNTRY: USA
(F) ZIP: 92121
- (v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
20 (B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30
- (vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER: US
(B) FILING DATE:
25 (C) CLASSIFICATION:
- (viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Burgoon, Richard P.
(B) REGISTRATION NUMBER: 34,787
- (ix) TELECOMMUNICATION INFORMATION:
30 (A) TELEPHONE: (858)453-7200
(B) TELEFAX: (858)453-7210

(2) INFORMATION FOR SEQ ID NO:1:

- (i) SEQUENCE CHARACTERISTICS:
35 (A) LENGTH: 1260 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

40 ATGGTCTTCT CGGCAGTGTT GACTGCGTTC CATACCGGGA CATCCAACAC AACATTTGTC 60

- 2 -

GTGTATGAAA ACACCTACAT GAATATTACA CTCCCTCCAC CATTCCAGCA TCCTGACCTC 120
AGTCCATTGC TTAGATATAG TTTTGAAACC ATGGCTCCCA CTGGTTTGAG TTCCTTGACC 180
GTGAATAGTA CAGCTGTGCC CACAACACCA GCAGCATTTA AGAGCCTAAA CTTGCCTCTT 240
CAGATCACCC TTTCTGCTAT AATGATATTC ATTCTGTTTG TGTCTTTTCT TGGGAAGTTG 300
5 GTTGTGTTGCC TCATGGTTTA CCAAAAAGCT GCCATGAGGT CTGCAATTAA CATCCTCCTT 360
GCCAGCCTAG CTTTGCAGA CATGTTGCTT GCAGTGCTGA ACATGCCCTT TGCCCTGGTA 420
ACTATTCTTA CTACCCGATG GATTTTTGGG AAATTCTTCT GTAGGGTATC TGCTATGTTT 480
TTCTGGTTAT TTGTGATAGA AGGAGTAGCC ATCCTGCTCA TCATTAGCAT AGATAGGTTT 540
CTTATTATAG TCCAGAGGCA GGATAAGCTA AACCCATATA GAGCTAAGGT TCTGATTGCA 600
10 GTTTCTTGGG CAACTTCCTT TTGTGTAGCT TTTCTTTTAG CCGTAGGAAA CCCCAGCTG 660
CAGATACCTT CCCGAGCTCC CCAGTGTGTG TTTGGGTACA CAACCAATCC AGGCTACCAG 720
GCTTATGTGA TTTTGATTTC TCTCATTTCT TTCTTCATAC CCTTCCTGGT AATACTGTAC 780
TCATTTATGG GCATACTCAA CACCCTTCGG CACAATGCCT TGAGGATCCA TAGCTACCCT 840
GAAGGTATAT GCCTCAGCCA GGCCAGCAAA CTGGGTCTCA TGAGTCTGCA GAGACCTTTC 900
15 CAGATGAGCA TTGACATGGG CTTTAAAACA CGTGCCTTCA CCACTATTTT GATTCTCTTT 960
GCTGTCTTCA TTGTCTGCTG GGCCCCATTC ACCACTTACA GCCTTGTGGC
AACATTCACT1020
AAGCACTTTT ACTATCAGCA CAACTTTTTT GAGATTAGCA CCTGGCTACT GTGGCTCTGC1080
TACCTCAAGT CTGCATTGAA TCCGCTGATC TACTACTGGA GGATTAAGAA ATTCCATGAT1140
20 GCTTGCCTGG ACATGATGCC TAAGTCCTTC AAGTTTTTGC CGCAGCTCCC TGGTCACACA1200
AAGCGACGGA TACGTCCTAG TGCTGTCTAT GTGTGTGGGG AACATCGGAC GGTGGTGTGA1260

(3) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 419 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

30 Met Val Phe Ser Ala Val Leu Thr Ala Phe His Thr Gly Thr Ser Asn
1 5 10 15

- 3 -

Thr Thr Phe Val Val Tyr Glu Asn Thr Tyr Met Asn Ile Thr Leu Pro
 20 25 30
 Pro Pro Phe Gln His Pro Asp Leu Ser Pro Leu Leu Arg Tyr Ser Phe
 35 40 45
 5 Glu Thr Met Ala Pro Thr Gly Leu Ser Ser Leu Thr Val Asn Ser Thr
 50 55 60
 Ala Val Pro Thr Thr Pro Ala Ala Phe Lys Ser Leu Asn Leu Pro Leu
 65 70 75 80
 10 Gln Ile Thr Leu Ser Ala Ile Met Ile Phe Ile Leu Phe Val Ser Phe
 85 90 95
 Leu Gly Asn Leu Val Val Cys Leu Met Val Tyr Gln Lys Ala Ala Met
 100 105 110
 Arg Ser Ala Ile Asn Ile Leu Leu Ala Ser Leu Ala Phe Ala Asp Met
 115 120 125
 15 Leu Leu Ala Val Leu Asn Met Pro Phe Ala Leu Val Thr Ile Leu Thr
 130 135 140
 Thr Arg Trp Ile Phe Gly Lys Phe Phe Cys Arg Val Ser Ala Met Phe
 145 150 155 160
 20 Phe Trp Leu Phe Val Ile Glu Gly Val Ala Ile Leu Leu Ile Ile Ser
 165 170 175
 Ile Asp Arg Phe Leu Ile Ile Val Gln Arg Gln Asp Lys Leu Asn Pro
 180 185 190
 Tyr Arg Ala Lys Val Leu Ile Ala Val Ser Trp Ala Thr Ser Phe Cys
 195 200 205
 25 Val Ala Phe Pro Leu Ala Val Gly Asn Pro Asp Leu Gln Ile Pro Ser
 210 215 220
 Arg Ala Pro Gln Cys Val Phe Gly Tyr Thr Thr Asn Pro Gly Tyr Gln
 225 230 235 240
 30 Ala Tyr Val Ile Leu Ile Ser Leu Ile Ser Phe Phe Ile Pro Phe Leu
 245 250 255
 Val Ile Leu Tyr Ser Phe Met Gly Ile Leu Asn Thr Leu Arg His Asn
 260 265 270
 Ala Leu Arg Ile His Ser Tyr Pro Glu Gly Ile Cys Leu Ser Gln Ala
 275 280 285
 35 Ser Lys Leu Gly Leu Met Ser Leu Gln Arg Pro Phe Gln Met Ser Ile
 290 295 300
 Asp Met Gly Phe Lys Thr Arg Ala Phe Thr Thr Ile Leu Ile Leu Phe

(4) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1119 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

| | | | | | | | |
|----|------------|------------|------------|------------|------------|------------|-----|
| | ATGTTAGCCA | ACAGCTCCTC | AACCAACAGT | TCTGTTCTCC | CGTGTCCTGA | CTACCGACCT | 60 |
| 25 | ACCCACCGCC | TGCACTTGGT | GGTCTACAGC | TTGGTGCTGG | CTGCCGGGCT | CCCCCTCAAC | 120 |
| | GCGCTAGCCC | TCTGGGTCTT | CCTGCGCGCG | CTGCGCGTGC | ACTCGGTGGT | GAGCGTGTA | 180 |
| | ATGTGTAACC | TGGCGGCCAG | CGACCTGCTC | TTCACCCTCT | CGCTGCCCCG | TCGTCTCTCC | 240 |
| | TACTACGCAC | TGCACCACTG | GCCCTTCCCC | GACCTCCTGT | GCCAGACGAC | GGGCGCCATC | 300 |
| | TTCCAGATGA | ACATGTACGG | CAGCTGCATC | TTCCTGATGC | TCATCAACGT | GGACCGCTAC | 360 |
| 30 | GCCGCCATCG | TGCACCGGCT | GCGACTGCGC | CACCTGCGGC | GGCCCCGCGT | GGCGCGGCTG | 420 |
| | CTCTGCCTGG | GCGTGTGGGC | GCTCATCCTG | GTGTTTGCCG | TGCCCCGCCG | CCGCGTGCA | 480 |
| | AGGCCCTCGC | GTTGCCGCTA | CCGGGACCTC | GAGGTGCGCC | TATGCTTCGA | GAGCTTCAGC | 540 |
| | GACGAGCTGT | GGAAAGGCAG | GCTGCTGCCC | CTCGTGCTGC | TGGCCGAGGC | GCTGGGCTTC | 600 |

- 5 -

CTGCTGCCCC TGGCGGCGGT GGTCTACTCG TCGGGCCGAG TCTTCTGGAC GCTGGCGCGC 660
 CCGGACGCCA CGCAGAGCCA GCGGCGGCGG AAGACCGTGC GCCTCCTGCT GGCTAACCTC 720
 GTCATCTTCC TGCTGTGCTT CGTGCCCTAC AACAGCACGC TGGCGGTCTA CGGGCTGCTG 780
 CGGAGCAAGC TGGTGGCGGC CAGCGTGCCT GCCCGCGATC GCGTGCGCGG GGTGCTGATG 840
 5 GTGATGGTGC TGCTGGCCGG CGCCAATGCG GTGCTGGACC CGCTGGTGTA CTACTTTAGC 900
 GCCGAGGGCT TCCGCAACAC CCTGCGCGGC CTGGGCACTC CGCACCGGGC CAGGACCTCG 960
 GCCACCAACG GGACGCGGGC GGCCTCGCG CAATCCGAAA GGTCGCGCGT CACCACCGAC1020
 GCCACCAGGC CGGATGCCGC CAGTCAGGGG CTGCTCCGAC CCTCCGACTC CCACTCTCTG1080
 TCTTCCTTCA CACAGTGTCC CCAGGATTCC GCCCTCTGA 1119

10 (5) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 372 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

15

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Met Leu Ala Asn Ser Ser Thr Asn Ser Ser Val Leu Pro Cys Pro
 1 5 10 15
 20 Asp Tyr Arg Pro Thr His Arg Leu His Leu Val Val Tyr Ser Leu Val
 20 25 30
 Leu Ala Ala Gly Leu Pro Leu Asn Ala Leu Ala Leu Trp Val Phe Leu
 35 40 45
 25 Arg Ala Leu Arg Val His Ser Val Val Ser Val Tyr Met Cys Asn Leu
 50 55 60
 Ala Ala Ser Asp Leu Leu Phe Thr Leu Ser Leu Pro Val Arg Leu Ser
 65 70 75 80
 Tyr Tyr Ala Leu His His Trp Pro Phe Pro Asp Leu Leu Cys Gln Thr
 85 90 95
 30 Thr Gly Ala Ile Phe Gln Met Asn Met Tyr Gly Ser Cys Ile Phe Leu
 100 105 110
 Met Leu Ile Asn Val Asp Arg Tyr Ala Ala Ile Val His Pro Leu Arg
 115 120 125

- 6 -

Leu Arg His Leu Arg Arg Pro Arg Val Ala Arg Leu Leu Cys Leu Gly
 130 135 140
 Val Trp Ala Leu Ile Leu Val Phe Ala Val Pro Ala Ala Arg Val His
 145 150 155 160
 5 Arg Pro Ser Arg Cys Arg Tyr Arg Asp Leu Glu Val Arg Leu Cys Phe
 165 170 175
 Glu Ser Phe Ser Asp Glu Leu Trp Lys Gly Arg Leu Leu Pro Leu Val
 180 185 190
 10 Leu Leu Ala Glu Ala Leu Gly Phe Leu Leu Pro Leu Ala Ala Val Val
 195 200 205
 Tyr Ser Ser Gly Arg Val Phe Trp Thr Leu Ala Arg Pro Asp Ala Thr
 210 215 220
 Gln Ser Gln Arg Arg Arg Lys Thr Val Arg Leu Leu Leu Ala Asn Leu
 225 230 235 240
 15 Val Ile Phe Leu Leu Cys Phe Val Pro Tyr Asn Ser Thr Leu Ala Val
 245 250 255
 Tyr Gly Leu Leu Arg Ser Lys Leu Val Ala Ala Ser Val Pro Ala Arg
 260 265 270
 20 Asp Arg Val Arg Gly Val Leu Met Val Met Val Leu Leu Ala Gly Ala
 275 280 285
 Asn Cys Val Leu Asp Pro Leu Val Tyr Tyr Phe Ser Ala Glu Gly Phe
 290 295 300
 Arg Asn Thr Leu Arg Gly Leu Gly Thr Pro His Arg Ala Arg Thr Ser
 305 310 315 320
 25 Ala Thr Asn Gly Thr Arg Ala Ala Leu Ala Gln Ser Glu Arg Ser Ala
 325 330 335
 Val Thr Thr Asp Ala Thr Arg Pro Asp Ala Ala Ser Gln Gly Leu Leu
 340 345 350
 30 Arg Pro Ser Asp Ser His Ser Leu Ser Ser Phe Thr Gln Cys Pro Gln
 355 360 365
 Asp Ser Ala Leu
 370

(6) INFORMATION FOR SEQ ID NO:5:

(1) SEQUENCE CHARACTERISTICS:

- 35 (A) LENGTH: 1107 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

- 7 -

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

ATGGCCAACCT CCACAGGGCT GAACGCCTCA GAAGTCGCAG GCTCGTTGGG GTTGATCCTG 60
GCAGCTGTCTG TGGAGGTGGG GGCAGTGTCTG GGCAACGGCG CGCTGCTGGT CGTGGTGCTG 120
5 CGCAGCGCCGG GACTGCGCGA CGCGCTCTAC CTGGCGCACC TGTGCGTCGT GGACCTGCTG 180
GCGGCCGCCT CCATCATGCC GCTGGGCGCTG CTGGCCGCAC CGCCGCCCGG GCTGGGCCCG 240
GTGCGCCTGG GCCCCGCGCC ATGCCGCGCC GCTCGCTTCC TCTCCGCCGC TCTGCTGCCG 300
GCCTGCACGC TCGGGGTGGC CGCACTTGGC CTGGCACGCT ACCGCCTCAT CGTGACCCCG 360
CTGCGGCCAG GCTCGCGGCC GCGCCTGTG CTCGTGCTCA CGCCCGTGTG GGCCGCGGCG 420
10 GGACTGCTGG GCGCGCTCTC CCTGCTCGGC CCGCCGCCCG CACCGCCCCC TGCTCCTGCT 480
CGCTGCTCGG TCCTGGCTGG GGGCCTCGGG CCCTTCCGGC CGCTCTGGGC CCTGCTGGCC 540
TTCGCGCTGC CCGCCCTCCT GCTGCTCGGC GCCTACGGCG GCATCTTCGT GGTGGCGCGT 600
CGCGCTGCCC TGAGGCCCCC ACGGCCGGCG CGCGGGTCCC GACTCCGCTC GGACTCTCTG 660
GATAGCCGCC TTTCATCTT GCCGCCGCTC CGGCCTCGCC TGCCCGGGGG CAAGGCGGCC 720
15 CTGGCCCCAG CGCTGGCCGT GGGCCAATTT GCAGCCTGCT GGCTGCCTTA TGGCTGCGCG 780
TGCCTGGCGC CCGCAGCGCG GGCCGCGGAA GCCGAAGCGG CTGTCACTG GTTCGCCTAC 840
TCGGCCTTCG CGGCTCAGCC CTTCCTGTAC GGGCTGCTGC AGCGCCCCGT GCGCTTGGCA 900
CTGGGCCGCC TCTCTCGCGG TGCACTGCCT GGACCTGTGC GGGCCTGCAC TCCGCAAGCC 960
TGGCACCCGC GGGCACTCTT GCAATGCCTC CAGAGACCCC CAGAGGGCCC TGCCGTAGGC 1020
20 CCTTCTGAGG CTCCAGAACA GACCCCGAG TTGGCAGGAG GGCGGAGCCC CGCATACCAG 1080
GGGCCACCTG AGAGTTCTCT CTCCTGA 1107

(7) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 368 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

- 8 -

Met Ala Asn Ser Thr Gly Leu Asn Ala Ser Glu Val Ala Gly Ser Leu
 1 5 10 15
 Gly Leu Ile Leu Ala Ala Val Val Glu Val Gly Ala Leu Leu Gly Asn
 20 25 30
 5 Gly Ala Leu Leu Val Val Val Leu Arg Thr Pro Gly Leu Arg Asp Ala
 35 40 45
 Leu Tyr Leu Ala His Leu Cys Val Val Asp Leu Leu Ala Ala Ala Ser
 50 55 60
 10 Ile Met Pro Leu Gly Leu Leu Ala Ala Pro Pro Pro Gly Leu Gly Arg
 65 70 75 80
 Val Arg Leu Gly Pro Ala Pro Cys Arg Ala Ala Arg Phe Leu Ser Ala
 85 90 95
 Ala Leu Leu Pro Ala Cys Thr Leu Gly Val Ala Ala Leu Gly Leu Ala
 100 105 110
 15 Arg Tyr Arg Leu Ile Val His Pro Leu Arg Pro Gly Ser Arg Pro Pro
 115 120 125
 Pro Val Leu Val Leu Thr Ala Val Trp Ala Ala Ala Gly Leu Leu Gly
 130 135 140
 20 Ala Leu Ser Leu Leu Gly Pro Pro Pro Ala Pro Pro Ala Pro Ala
 145 150 155 160
 Arg Cys Ser Val Leu Ala Gly Gly Leu Gly Pro Phe Arg Pro Leu Trp
 165 170 175
 Ala Leu Leu Ala Phe Ala Leu Pro Ala Leu Leu Leu Leu Gly Ala Tyr
 180 185 190
 25 Gly Gly Ile Phe Val Val Ala Arg Arg Ala Ala Leu Arg Pro Pro Arg
 195 200 205
 Pro Ala Arg Gly Ser Arg Leu Arg Ser Asp Ser Leu Asp Ser Arg Leu
 210 215 220
 30 Ser Ile Leu Pro Pro Leu Arg Pro Arg Leu Pro Gly Gly Lys Ala Ala
 225 230 235 240
 Leu Ala Pro Ala Leu Ala Val Gly Gln Phe Ala Ala Cys Trp Leu Pro
 245 250 255
 Tyr Gly Cys Ala Cys Leu Ala Pro Ala Ala Arg Ala Ala Glu Ala Glu
 260 265 270
 35 Ala Ala Val Thr Trp Val Ala Tyr Ser Ala Phe Ala Ala His Pro Phe
 275 280 285
 Leu Tyr Gly Leu Leu Gln Arg Pro Val Arg Leu Ala Leu Gly Arg Leu

290 295 300
 Ser Arg Arg Ala Leu Pro Gly Pro Val Arg Ala Cys Thr Pro Gln Ala
 305 310 315 320
 Trp His Pro Arg Ala Leu Leu Gln Cys Leu Gln Arg Pro Pro Glu Gly
 5 325 330 335
 Pro Ala Val Gly Pro Ser Glu Ala Pro Glu Gln Thr Pro Glu Leu Ala
 340 345 350
 Gly Gly Arg Ser Pro Ala Tyr Gln Gly Pro Pro Glu Ser Ser Leu Ser
 355 360 365

10 (8) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1008 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 15 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

ATGGAATCAT CTTTCTCATT TGGAGTGATC CTTGCTGTCC TGGCCTCCCT CATCATTGCT 60
 ACTAACACAC TAGTGGCTGT GGCTGTGCTG CTGTTGATCC ACAAGAATGA TGGTGTCACT 120
 20 CTCTGCTTCA CCTTGAATCT GGCTGTGGCT GACACCTTGA TTGGTGTGGC CATCTCTGGC 180
 CTACTCACAG ACCAGCTCTC CAGCCCTTCT CGGCCACAC AGAAGACCCT GTGCAGCCTG 240
 CGGATGGCAT TTGTCACTTC CTCCGCAGCT GCCTCTGTCC TCACGGTCAT GCTGATCACC 300
 TTTGACAGGT ACCTTGCCAT CAAGCAGCCC TTCCGCTACT TGAAGATCAT GAGTGGGTTC 360
 GTGGCCGGGG CCTGCATTGC CGGGCTGTGG TTAGTGTCTT ACCTCATTGG CTTCTCTCCA 420
 25 CTCGGAATCC CCATGTTCCA GCAGACTGCC TACAAAGGGC AGTGCAGCTT CTTTGCTGTA 480
 TTTCACCTTC ACTTCGTGCT GACCCTCTCC TGCCTTGGCT TCTTCCCAGC CATGCTCCTC 540
 TTTGTCTTCT TCTACTGCGA CATGCTCAAG ATTGCCTCCA TGCACAGCCA GCAGATTCTA 600
 AAGATGGAAC ATGCAGGAGC CATGGCTGGA GGTATCGAT CCCCACGGAC TCCCAGCGAC 660
 TTCAAAGCTC TCCGTACTGT GTCTGTTCTC ATTGGGAGCT TTGCTCTATC CTGGACCCCC 720
 30 TTCCTTATCA CTGGCATTGT GCAGGTGGCC TGCCAGGAGT GTCACCTCTA CCTAGTGCTG 780
 GAACGGTACC TGTGGCTGCT CGGCGTGGGC AACTCCCTGC TCAACCCACT CATCTATGCC 840

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TATTGGCAGA AGGAGGTGCG ACTGCAGCTC TACCACATGG CCCTAGGAGT GAAGAAGGTG 900
 CTCACCTCAT TCCTCCTCTT TCTCTCGGCC AGGAATTGTG GCCCAGAGAG GCCCAGGGAA 960
 AGTTCCTGTC ACATCGTCAC TATCTCCAGC TCAGAGTTTG ATGGCTAA 1008

(9) INFORMATION FOR SEQ ID NO:8:

- 5 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 335 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant
- 10 (ii) MOLECULE TYPE: protein
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:
- | | | | | | | | | | | | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|--|
| | Met | Glu | Ser | Ser | Phe | Ser | Phe | Gly | Val | Ile | Leu | Ala | Val | Leu | Ala | Ser | |
| | 1 | | | | 5 | | | | | 10 | | | | | 15 | | |
| 15 | Leu | Ile | Ile | Ala | Thr | Asn | Thr | Leu | Val | Ala | Val | Ala | Val | Leu | Leu | Leu | |
| | | | | 20 | | | | 25 | | | | | | 30 | | | |
| | Ile | His | Lys | Asn | Asp | Gly | Val | Ser | Leu | Cys | Phe | Thr | Leu | Asn | Leu | Ala | |
| | | | 35 | | | | 40 | | | | | | 45 | | | | |
| | Val | Ala | Asp | Thr | Leu | Ile | Gly | Val | Ala | Ile | Ser | Gly | Leu | Leu | Thr | Asp | |
| | | | 50 | | | | 55 | | | | | 60 | | | | | |
| 20 | Gln | Leu | Ser | Ser | Pro | Ser | Arg | Pro | Thr | Gln | Lys | Thr | Leu | Cys | Ser | Leu | |
| | 65 | | | | | 70 | | | | 75 | | | | | 80 | | |
| | Arg | Met | Ala | Phe | Val | Thr | Ser | Ser | Ala | Ala | Ala | Ser | Val | Leu | Thr | Val | |
| | | | | | 85 | | | | 90 | | | | | 95 | | | |
| 25 | Met | Leu | Ile | Thr | Phe | Asp | Arg | Tyr | Leu | Ala | Ile | Lys | Gln | Pro | Phe | Arg | |
| | | | | 100 | | | | | 105 | | | | | 110 | | | |
| | Tyr | Leu | Lys | Ile | Met | Ser | Gly | Phe | Val | Ala | Gly | Ala | Cys | Ile | Ala | Gly | |
| | | | 115 | | | | 120 | | | | | | 125 | | | | |
| | Leu | Trp | Leu | Val | Ser | Tyr | Leu | Ile | Gly | Phe | Leu | Pro | Leu | Gly | Ile | Pro | |
| | | | 130 | | | | 135 | | | | | 140 | | | | | |
| 30 | Met | Phe | Gln | Gln | Thr | Ala | Tyr | Lys | Gly | Gln | Cys | Ser | Phe | Phe | Ala | Val | |
| | 145 | | | | | 150 | | | | | 155 | | | | 160 | | |
| | Phe | His | Pro | His | Phe | Val | Leu | Thr | Leu | Ser | Cys | Val | Gly | Phe | Phe | Pro | |
| | | | | | 165 | | | | 170 | | | | | 175 | | | |
| 35 | Ala | Met | Leu | Leu | Phe | Val | Phe | Phe | Tyr | Cys | Asp | Met | Leu | Lys | Ile | Ala | |
| | | | | 180 | | | | | 185 | | | | | 190 | | | |

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Ser Met His Ser Gln Gln Ile Arg Lys Met Glu His Ala Gly Ala Met
 195 200 205

Ala Gly Gly Tyr Arg Ser Pro Arg Thr Pro Ser Asp Phe Lys Ala Leu
 210 215 220

5 Arg Thr Val Ser Val Leu Ile Gly Ser Phe Ala Leu Ser Trp Thr Pro
 225 230 235 240

Phe Leu Ile Thr Gly Ile Val Gln Val Ala Cys Gln Glu Cys His Leu
 245 250 255

10 Tyr Leu Val Leu Glu Arg Tyr Leu Trp Leu Leu Gly Val Gly Asn Ser
 260 265 270

Leu Leu Asn Pro Leu Ile Tyr Ala Tyr Trp Gln Lys Glu Val Arg Leu
 275 280 285

Gln Leu Tyr His Met Ala Leu Gly Val Lys Lys Val Leu Thr Ser Phe
 290 295 300

15 Leu Leu Phe Leu Ser Ala Arg Asn Cys Gly Pro Glu Arg Pro Arg Glu
 305 310 315 320

Ser Ser Cys His Ile Val Thr Ile Ser Ser Ser Glu Phe Asp Gly
 325 330 335

(10) INFORMATION FOR SEQ ID NO:9:

- 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1413 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

- 25 (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

ATGGACACTA CCATGGAAGC TGACCTGGGT GCCACTGGCC ACAGGCCCCG CACAGAGCTT 60
 GATGATGAGG ACTCCTACCC CCAAGGTGGC TGGGACACGG TCTTCCCTGGT GGCCCTGCTG 120
 CTCCTTGGGC TGCCAGCCAA TGGGTGTATG GCGTGGCTGG CCGGCTCCCA GGCCCGGCAT 180
 30 GGAGCTGGCA CGCGTCTGGC GCTGCTCCTG CTCAGCCTGG CCCTCTCTGA CTTCTTGTTT 240
 CTGGCAGCAG CGGCCTTCCA GATCCTAGAG ATCCGGCATG GGGGACACTG GCCGCTGGGG 300
 ACAGCTGCCT GCCGCTTCTA CTACTTCCTA TGGGGCGTGT CCTACTCCTC CGGCCTCTTC 360
 CTGCTGGCCG CCCTCAGCCT CGACCGCTGC CTGCTGGCGC TGTGCCCACA CTGGTACCCT 420
 GGGCACCGCC CAGTCCGCCT GCCCTCTGG GTCTGCGCCG GTGTCTGGGT GCTGGCCACA 480

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CTCTTCAGCG TGCCCTGGCT GGTCTTCCCC GAGGCTGCCG TCTGGTGGTA CGACCTGGTC 540
 ATCTGCCTGG ACTTCTGGGA CAGCGAGGAG CTGTCGCTGA GGATGCTGGA GGTCTGGGG 600
 GGCTTCCTGC CTTTCCTCCT GCTGCTCGTC TGCCACGTGC TCACCCAGGC CACAGCCTGT 660
 CGCACCTGCC ACCGCCAACA GCAGCCCGCA GCCTGCCGGG GCTTCGCCCG TGTGGCCAGG 720
 5 ACCATTCTGT CAGCCTATGT GGTCTGAGG CTGCCCTACC AGCTGGCCCA GCTGCTCTAC 780
 CTGGCCTTCC TGTGGGACGT CTACTCTGGC TACCTGCTCT GGGAGGCCCT GGTCTACTCC 840
 GACTACCTGA TCCTACTCAA CAGCTGCCTC AGCCCCCTCC TCTGCCTCAT GGCCAGTGCC 900
 GACCTCCGGA CCCTGCTGCG CTCCGTGCTC TCGTCCTTCG CGGCAGCTCT CTGCGAGGAG 960
 CGGCCGGGCA GCTTCACGCC CACTGAGCCA CAGACCCAGC TAGATTCTGA GGGTCCAAC1020
 10 CTGCCAGAGC CGATGGCAGA GGCCAGTCA CAGATGGATC CTGTGGCCCA GCCTCAGGTG1080
 AACCCACAC TCCAGCCAG ATCGGATCCC ACAGCTCAGC CACAGCTGAA CCCTACGGCC1140
 CAGCCACAGT CGGATCCCAC AGCCAGCCA CAGCTGAACC TCATGGCCCA GCCACAGTCA1200
 GATTCTGTGG CCCAGCCACA GGCAGACACT AACGTCCAGA CCCCTGCACC TGCTGCCAGT1260
 TCTGTGCCCA GTCCCTGTGA TGAAGCTTCC CCAACCCCAT CCTCGCATCC TACCCAGGG1320
 15 GCCCTTGAGG ACCCAGCCAC ACCTCCTGCC TCTGAAGGAG AAAGCCCCAG CAGCACCCCG1380
 CCAGAGGCGG CCCC GGCGC AGGCCCCACG TGA 1413

(11) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 468 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

25 Met Asp Thr Thr Met Glu Ala Asp Leu Gly Ala Thr Gly His Arg Pro
 1 5 10 15
 Arg Thr Glu Leu Asp Asp Glu Asp Ser Tyr Pro Gln Gly Gly Trp Asp
 20 25 30
 Thr Val Phe Leu Val Ala Leu Leu Leu Gly Leu Pro Ala Asn Gly
 30 35 40 45
 Leu Met Ala Trp Leu Ala Gly Ser Gln Ala Arg His Gly Ala Gly Thr

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| | | | | | | | | | | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| | 50 | | 55 | | 60 | | | | | | | | | | | |
| | Arg | Leu | Ala | Leu | Leu | Leu | Leu | Ser | Leu | Ala | Leu | Ser | Asp | Phe | Leu | Phe |
| | 65 | | | | 70 | | | | | | 75 | | | | | 80 |
| 5 | Leu | Ala | Ala | Ala | Ala | Phe | Gln | Ile | Leu | Glu | Ile | Arg | His | Gly | Gly | His |
| | | | | | 85 | | | | | 90 | | | | | 95 | |
| | Trp | Pro | Leu | Gly | Thr | Ala | Ala | Cys | Arg | Phe | Tyr | Tyr | Phe | Leu | Trp | Gly |
| | | | | 100 | | | | | 105 | | | | | | 110 | |
| | Val | Ser | Tyr | Ser | Ser | Gly | Leu | Phe | Leu | Leu | Ala | Ala | Leu | Ser | Leu | Asp |
| | | | 115 | | | | | 120 | | | | | | 125 | | |
| 10 | Arg | Cys | Leu | Leu | Ala | Leu | Cys | Pro | His | Trp | Tyr | Pro | Gly | His | Arg | Pro |
| | | 130 | | | | | 135 | | | | | 140 | | | | |
| | Val | Arg | Leu | Pro | Leu | Trp | Val | Cys | Ala | Gly | Val | Trp | Val | Leu | Ala | Thr |
| | 145 | | | | 150 | | | | | | 155 | | | | | 160 |
| 15 | Leu | Phe | Ser | Val | Pro | Trp | Leu | Val | Phe | Pro | Glu | Ala | Ala | Val | Trp | Trp |
| | | | | | 165 | | | | | 170 | | | | | 175 | |
| | Tyr | Asp | Leu | Val | Ile | Cys | Leu | Asp | Phe | Trp | Asp | Ser | Glu | Glu | Leu | Ser |
| | | | 180 | | | | | | 185 | | | | | 190 | | |
| | Leu | Arg | Met | Leu | Glu | Val | Leu | Gly | Gly | Phe | Leu | Pro | Phe | Leu | Leu | Leu |
| | | | 195 | | | | | 200 | | | | | 205 | | | |
| 20 | Leu | Val | Cys | His | Val | Leu | Thr | Gln | Ala | Thr | Arg | Thr | Cys | His | Arg | Gln |
| | | 210 | | | | | 215 | | | | | 220 | | | | |
| | Gln | Gln | Pro | Ala | Ala | Cys | Arg | Gly | Phe | Ala | Arg | Val | Ala | Arg | Thr | Ile |
| | 225 | | | | | 230 | | | | | 235 | | | | 240 | |
| 25 | Leu | Ser | Ala | Tyr | Val | Val | Leu | Arg | Leu | Pro | Tyr | Gln | Leu | Ala | Gln | Leu |
| | | | | 245 | | | | | | 250 | | | | | 255 | |
| | Leu | Tyr | Leu | Ala | Phe | Leu | Trp | Asp | Val | Tyr | Ser | Gly | Tyr | Leu | Leu | Trp |
| | | | 260 | | | | | 265 | | | | | | 270 | | |
| | Glu | Ala | Leu | Val | Tyr | Ser | Asp | Tyr | Leu | Ile | Leu | Leu | Asn | Ser | Cys | Leu |
| | | | 275 | | | | | 280 | | | | | 285 | | | |
| 30 | Ser | Pro | Phe | Leu | Cys | Leu | Met | Ala | Ser | Ala | Asp | Leu | Arg | Thr | Leu | Leu |
| | | 290 | | | | | 295 | | | | | 300 | | | | |
| | Arg | Ser | Val | Leu | Ser | Ser | Phe | Ala | Ala | Ala | Leu | Cys | Glu | Glu | Arg | Pro |
| | 305 | | | | | 310 | | | | | 315 | | | | 320 | |
| 35 | Gly | Ser | Phe | Thr | Pro | Thr | Glu | Pro | Gln | Thr | Gln | Leu | Asp | Ser | Glu | Gly |
| | | | | 325 | | | | | 330 | | | | | | 335 | |
| | Pro | Thr | Leu | Pro | Glu | Pro | Met | Ala | Glu | Ala | Gln | Ser | Gln | Met | Asp | Pro |
| | | | 340 | | | | | 345 | | | | | 350 | | | |

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Val Ala Gln Pro Gln Val Asn Pro Thr Leu Gln Pro Arg Ser Asp Pro
 355 360 365

Thr Ala Gln Pro Gln Leu Asn Pro Thr Ala Gln Pro Gln Ser Asp Pro
 370 375 380

5 Thr Ala Gln Pro Gln Leu Asn Leu Met Ala Gln Pro Gln Ser Asp Ser
 385 390 395 400

Val Ala Gln Pro Gln Ala Asp Thr Asn Val Gln Thr Pro Ala Pro Ala
 405 410 415

10 Ala Ser Ser Val Pro Ser Pro Cys Asp Glu Ala Ser Pro Thr Pro Ser
 420 425 430

Ser His Pro Thr Pro Gly Ala Leu Glu Asp Pro Ala Thr Pro Pro Ala
 435 440 445

Ser Glu Gly Glu Ser Pro Ser Ser Thr Pro Pro Glu Ala Ala Pro Gly
 450 455 460

15 Ala Gly Pro Thr
 465

(12) INFORMATION FOR SEQ ID NO:11:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 1248 base pairs
- 20 (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

25 ATGTCAGGGA TGA AAAACT TCAGAATGCT TCCTGGATCT ACCAGCAGAA ACTAGAAGAT 60

CCATTCCAGA AACACCTGAA CAGCACCGAG GAGTATCTGG CCTTCCTCTG CGGACCTCGG 120

CGCAGCCACT TCTTCCTCCC CGTGTCTGTG GTGTATGTGC CAATTTTGT GGTGGGGGTC 180

ATTGGCAATG TCCTGGTGTG CCTGGTGATT CTGCAGCACC AGGCTATGAA GACGCCCACC 240

AACTACTACC TCTTCAGCCT GGCGGTCTCT GACCTCCTGG TCCTGCTCCT TGGAAATGCCC 300

30 CTGGAGGTCT ATGAGATGTG GCGCAACTAC CCTTCTTGT TCGGGCCCGT GGGCTGTCTAC 360

TTCAAGACGG CCCTCTTTGA GACCGTGTGC TTCGCCTCCA TCCTCAGCAT CACCACCGTC 420

AGCGTGGAGC GCTACGTGGC CATCCTACAC CCGTTCGCG CCAAAGTCA GAGCACCCGG 480

CGCCGGGCCC TCAGGATCCT CGGCATCGTC TGGGGCTTCT CCGTGCTCTT CTCCCTGCCC 540

AACACCAGCA TCCATGGCAT CAAGTTCCAC TACTTCCCCA ATGGGTCCCCT GGTCCCAGGT 600
 TCGGCCACCT GTACGGTCAT CAAGCCCATG TGGATCTACA ATTTCATCAT CCAGGTCACC 660
 TCCTTCCTAT TCTACCTCCT CCCCATGACT GTCATCAGTG TCCTCTACTA CCTCATGGCA 720
 CTCAGACTAA AGAAAGACAA ATCTCTTGAG GCAGATGAAG GGAATGCAAA TATTCAAAGA 780
 5 CCCTGCAGAA AATCAGTCAA CAAGATGCTG TTTGTCTTGG TCTTAGTGTT TGCTATCTGT 840
 TGGGCCCCGT TCCACATGA CCGACTCTTC TTCAGCTTTG TGGAGGAGTG GAGTGAATCC 900
 CTGGCTGCTG TGTTC AACCT CGTCCATGTG GTGTCAGGTG TCTTCTTCTA CCTGAGCTCA 960
 GCTGTCAACC CCATTATCTA TAACCTACTG TCTCGCCGCT TCCAGGCAGC ATTCCAGAAT1020
 GTGATCTCTT CTTTCCACAA ACAGTGGCAC TCCCAGCATG ACCCAGATT GCCACCTGCC1080
 10 CAGCGGAACA TCTTCCTGAC AGAATGCCAC TTTGTGGAGC TGACCGAAGA TATAGGTCCC1140
 CAATTCCCAT GTCAGTCATC CATGCACAAC TCTCACCTCC CAACAGCCCT CTCTAGTGAA1200
 CAGATGTCAA GAACAACTA TCAAAGCTTC CACTTTAACA AAACCTGA 1248

(13) INFORMATION FOR SEQ ID NO:12:

- (i) SEQUENCE CHARACTERISTICS:
- 15 (A) LENGTH: 415 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant
- (ii) MOLECULE TYPE: protein
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:
- | | | | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Met | Ser | Gly | Met | Glu | Lys | Leu | Gln | Asn | Ala | Ser | Trp | Ile | Tyr | Gln | Gln |
| 1 | | | | | 5 | | | | 10 | | | | | 15 | |
| Lys | Leu | Glu | Asp | Pro | Phe | Gln | Lys | His | Leu | Asn | Ser | Thr | Glu | Glu | Tyr |
| | | | 20 | | | | 25 | | | | | | 30 | | |
| Leu | Ala | Phe | Leu | Cys | Gly | Pro | Arg | Arg | Ser | His | Phe | Phe | Leu | Pro | Val |
| | | | 35 | | | | 40 | | | | | | 45 | | |
| Ser | Val | Val | Tyr | Val | Pro | Ile | Phe | Val | Val | Gly | Val | Ile | Gly | Asn | Val |
| | | | 50 | | | | 55 | | | | | 60 | | | |
| Leu | Val | Cys | Leu | Val | Ile | Leu | Gln | His | Gln | Ala | Met | Lys | Thr | Pro | Thr |
| | | | 65 | | | 70 | | | | 75 | | | | 80 | |
| Asn | Tyr | Tyr | Leu | Phe | Ser | Leu | Ala | Val | Ser | Asp | Leu | Leu | Val | Leu | Leu |
| | | | 85 | | | | | | 90 | | | | | 95 | |

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Leu Gly Met Pro Leu Glu Val Tyr Glu Met Trp Arg Asn Tyr Pro Phe
 100 105 110

Leu Phe Gly Pro Val Gly Cys Tyr Phe Lys Thr Ala Leu Phe Glu Thr
 115 120 125

5 Val Cys Phe Ala Ser Ile Leu Ser Ile Thr Thr Val Ser Val Glu Arg
 130 135 140

Tyr Val Ala Ile Leu His Pro Phe Arg Ala Lys Leu Gln Ser Thr Arg
 145 150 155 160

10 Arg Arg Ala Leu Arg Ile Leu Gly Ile Val Trp Gly Phe Ser Val Leu
 165 170 175

Phe Ser Leu Pro Asn Thr Ser Ile His Gly Ile Lys Phe His Tyr Phe
 180 185 190

Pro Asn Gly Ser Leu Val Pro Gly Ser Ala Thr Cys Thr Val Ile Lys
 195 200 205

15 Pro Met Trp Ile Tyr Asn Phe Ile Ile Gln Val Thr Ser Phe Leu Phe
 210 215 220

Tyr Leu Leu Pro Met Thr Val Ile Ser Val Leu Tyr Tyr Leu Met Ala
 225 230 235 240

20 Leu Arg Leu Lys Lys Asp Lys Ser Leu Glu Ala Asp Glu Gly Asn Ala
 245 250 255

Asn Ile Gln Arg Pro Cys Arg Lys Ser Val Asn Lys Met Leu Phe Val
 260 265 270

Leu Val Leu Val Phe Ala Ile Cys Trp Ala Pro Phe His Ile Asp Arg
 275 280 285

25 Leu Phe Phe Ser Phe Val Glu Glu Trp Ser Glu Ser Leu Ala Ala Val
 290 295 300

Phe Asn Leu Val His Val Val Ser Gly Val Phe Phe Tyr Leu Ser Ser
 305 310 315 320

30 Ala Val Asn Pro Ile Ile Tyr Asn Leu Leu Ser Arg Arg Phe Gln Ala
 325 330 335

Ala Phe Gln Asn Val Ile Ser Ser Phe His Lys Gln Trp His Ser Gln
 340 345 350

His Asp Pro Gln Leu Pro Pro Ala Gln Arg Asn Ile Phe Leu Thr Glu
 355 360 365

35 Cys His Phe Val Glu Leu Thr Glu Asp Ile Gly Pro Gln Phe Pro Cys
 370 375 380

Gln Ser Ser Met His Asn Ser His Leu Pro Thr Ala Leu Ser Ser Glu
 385 390 395 400

Gln Met Ser Arg Thr Asn Tyr Gln Ser Phe His Phe Asn Lys Thr
 405 410 415

(14) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1173 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

ATGCCAGATA CTAATAGCAC AATCAATTTA TCACTAAGCA CTCGTGTTAC TTTAGCATTT 60
 TTTATGTCCT TAGTAGCTTT TGCTATAATG CTAGGAAATG CTTTGGTCAT TTTAGCTTTT 120
 GTGGTGGACA AAAACCTTAG ACATCGAAGT AGTTATTTTT TTCTTAACTT GGCCATCTCT 180
 GACTTCTTTG TGGGTGTGAT CTCATTCTCT TTGTACATCC CTCACACGCT GTTCGAATGG 240
 15 GATTTTGGAA AGGAAATCTG TGTATTTTGG CTCACTACTG ACTATCTGTT ATGTACAGCA 300
 TCTGTATATA ACATTGTCCT CATCAGCTAT GATCGATACC TGTCAGTCTC AAATGCTGTG 360
 TCTTATAGAA CTCAACATAC TGGGGTCTTG AAGATTGTTA CTCTGATGGT GGCCGTTTGG 420
 GTGCTGGCCT TCTTAGTGAA TGGGCCAATG ATTCTAGTTT CAGAGTCTTG GAAGGATGAA 480
 GGTAGTGAAT GTGAACCTGG ATTTTTTTCG GAATGGTACA TCCTTGCCAT CACATCATTC 540
 20 TTGGAATTCG TGATCCCACT CATCTTAGTC GCTTATTTCA ACATGAATAT TTATTGGAGC 600
 CTGTGGAAGC GTGATCATCT CAGTAGGTGC CAAAGCCATC CTGGACTGAC TGCTGTCTCT 660
 TCCAACATCT GTGGACACTC ATTCAGAGGT AGACTATCTT CAAGGAGATC TCTTTCTGCA 720
 TCGACAGAAG TTCCTGCATC CTTTCATTCA GAGAGACAGA GGAGAAAGAG TAGTCTCATG 780
 TTTTCTCAA GAACCAAGAT GAATAGCAAT ACAATTGCTT CAAAATGGG TTCCTTCTCC 840
 25 CAATCAGATT CTGTAGCTCT TCACCAAAGG GAACATGTTG AACTGCTTAG AGCCAGGAGA 900
 TTAGCCAAGT CACTGGCCAT TCTCTTAGGG GTTTTGTCTG TTTGCTGGGC TCCATATTCT 960
 CTGTTCAACA TTGTCCTTTC ATTTTATTCC TCAGCAACAG GTCCTAAATC AGTTTGGTAT 1020
 AGAATTGCAT TTTGGCTTCA GTGGTTCAAT TCCTTTGTCA ATCCTCTTTT GTATCCATTG 1080
 TGTCAACAAGC GCTTTCAAAA GGCTTCTCTG AAAATATTTT GTATAAAAAA GCAACCTCTA 1140
 30 CCATCACAAC ACAGTCGGTC AGTATCTTCT TAA -1173

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(15) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 390 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

```

10 Met Pro Asp Thr Asn Ser Thr Ile Asn Leu Ser Leu Ser Thr Arg Val
    1           5           10           15

    Thr Leu Ala Phe Phe Met Ser Leu Val Ala Phe Ala Ile Met Leu Gly
        20           25           30

    Asn Ala Leu Val Ile Leu Ala Phe Val Val Asp Lys Asn Leu Arg His
        35           40           45

15 Arg Ser Ser Tyr Phe Phe Leu Asn Leu Ala Ile Ser Asp Phe Phe Val
    50           55           60

    Gly Val Ile Ser Ile Pro Leu Tyr Ile Pro His Thr Leu Phe Glu Trp
    65           70           75           80

20 Asp Phe Gly Lys Glu Ile Cys Val Phe Trp Leu Thr Thr Asp Tyr Leu
        85           90           95

    Leu Cys Thr Ala Ser Val Tyr Asn Ile Val Leu Ile Ser Tyr Asp Arg
        100          105          110

    Tyr Leu Ser Val Ser Asn Ala Val Ser Tyr Arg Thr Gln His Thr Gly
        115          120          125

25 Val Leu Lys Ile Val Thr Leu Met Val Ala Val Trp Val Leu Ala Phe
    130          135          140

    Leu Val Asn Gly Pro Met Ile Leu Val Ser Glu Ser Trp Lys Asp Glu
    145          150          155          160

30 Gly Ser Glu Cys Glu Pro Gly Phe Phe Ser Glu Trp Tyr Ile Leu Ala
        165          170          175

    Ile Thr Ser Phe Leu Glu Phe Val Ile Pro Val Ile Leu Val Ala Tyr
        180          185          190

    Phe Asn Met Asn Ile Tyr Trp Ser Leu Trp Lys Arg Asp His Leu Ser
        195          200          205

35 Arg Cys Gln Ser His Pro Gly Leu Thr Ala Val Ser Ser Asn Ile Cys
    210          215          220

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Gly His Ser Phe Arg Gly Arg Leu Ser Ser Arg Arg Ser Leu Ser Ala
 225 230 235 240
 Ser Thr Glu Val Pro Ala Ser Phe His Ser Glu Arg Gln Arg Arg Lys
 245 250 255
 5 Ser Ser Leu Met Phe Ser Ser Arg Thr Lys Met Asn Ser Asn Thr Ile
 260 265 270
 Ala Ser Lys Met Gly Ser Phe Ser Gln Ser Asp Ser Val Ala Leu His
 275 280 285
 10 Gln Arg Glu His Val Glu Leu Leu Arg Ala Arg Arg Leu Ala Lys Ser
 290 295 300
 Leu Ala Ile Leu Leu Gly Val Phe Ala Val Cys Trp Ala Pro Tyr Ser
 305 310 315 320
 Leu Phe Thr Ile Val Leu Ser Phe Tyr Ser Ser Ala Thr Gly Pro Lys
 325 330 335
 15 Ser Val Trp Tyr Arg Ile Ala Phe Trp Leu Gln Trp Phe Asn Ser Phe
 340 345 350
 Val Asn Pro Leu Leu Tyr Pro Leu Cys His Lys Arg Phe Gln Lys Ala
 355 360 365
 20 Phe Leu Lys Ile Phe Cys Ile Lys Lys Gln Pro Leu Pro Ser Gln His
 370 375 380
 Ser Arg Ser Val Ser Ser
 385 390

(16) INFORMATION FOR SEQ ID NO:15:

- (i) SEQUENCE CHARACTERISTICS:
 25 (A) LENGTH: 1128 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

ATGGCGAACG CGAGCGAGCC GGGTGGCAGC GCGCGCGGCG AGGCGGCCGC CCTGGGCCTC 60
 AAGCTGGCCA CGCTCAGCCT GCTGCTGTGC GTGAGCCTAG CCGGCAACGT GCTGTTCGCG 120
 CTGCTGATCG TGCGGGAGCG CAGCCTGCAC CGCGCCCCGT ACTACCTGCT GCTCGACCTG 180
 TGCCTGGCCG ACGGGCTGCG CGCGCTCGCC TGCCTCCCGG CCGTCATGCT GGCGGCGCGG 240
 35 CGTGCGGCGG CCGCGGCGGG GCGCCGCGG GCGCGCTGG GCTGCAAGCT GCTCGCCTTC 300

- 20 -

CTGGCCGCGC TCTTCTGCTT CCACGCCGCC TTCCTGCTGC TGGGCGTGGG CGTCACCCGC 360
TACCTGGCCA TCGCGCACCA CCGCTTCTAT GCAGAGCGCC TGGCCGGCTG GCCGTGCGCC 420
GCCATGCTGG TGTGCGCCGC CTGGGCGCTG GCGCTGGCCG CGGCCTTCCC GCCAGTGCTG 480
GACGGCGGTG GCGACGACGA GGACGCGCCG TCGGCCCTGG AGCAGCGGCC CGACGGCGCC 540
5 CCCGGCGCGC TGGGCTTCCT GCTGCTGCTG GCCGTGGTGG TGGGCGCCAC GCACCTCGTC 600
TACCTCCGCC TGCTCTTCTT CATCCACGAC CGCCGCAAGA TGCGGCCCGC GCGCCTGGTG 660
CCCCCGTCA GCCACGACTG GACCTTCCAC GGCCCGGGCG CCACCGGCCA GCGGCCGCC 720
AACTGGACGG CGGGCTTCGG CCGCGGGCCC ACGCCGCCCG CGCTTGTGGG CATCCGGCCC 780
GCAGGGCCGG GCCCGGGCG GCGCCGCCTC CTCGTGCTGG AAGAATTCAA GACGGAGAAG 840
10 AGGCTGTGCA AGATGTTCTA CGCCGTCACG CTGCTCTTCC TGCTCCTCTG GGGGCCCTAC 900
GTCGTGGCCA GCTACCTGCG GGTCTGGTG CGGCCCGCG CCGTCCCCCA GGCCTACCTG 960
ACGGCCTCCG TGTGGCTGAC CTTGCGCAG GCCGCGATCA ACCCGTCGT GTGCTTCTC 1020
TTCAACAGGG AGCTGAGGGA CTGCTTCAGG GCCCAGTTCC CCTGTGCCA GAGCCCCCG 1080
ACCACCCAGG CGACCCATCC CTGCGACCTG AAAGGCATTG GTTTATGA 1128

15 (17) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 375 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:
20 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

Met Ala Asn Ala Ser Glu Pro Gly Gly Ser Gly Gly Glu Ala Ala
1 5 10 15
25 Ala Leu Gly Leu Lys Leu Ala Thr Leu Ser Leu Leu Leu Cys Val Ser
20 25 30
Leu Ala Gly Asn Val Leu Phe Ala Leu Leu Ile Val Arg Glu Arg Ser
35 40 45
30 Leu His Arg Ala Pro Tyr Tyr Leu Leu Leu Asp Leu Cys Leu Ala Asp
50 55 60
Gly Leu Arg Ala Leu Ala Cys Leu Pro Ala Val Met Leu Ala Ala Arg
65 70 75 80

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370

375

(18) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1002 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

10 ATGAACACCA CAGTGATGCA AGGCTTCAAC AGATCTGAGC GGTGCCCCAG AGACACTCGG 60
ATAGTACAGC TGGTATTCCC AGCCCTCTAC ACAGTGGTTT TCTTGACCGG CATCCTGCTG 120
AATACTTTGG CTCTGTGGGT GTTGTTCAC ATCCCCAGCT CCTCCACCTT CATCATCTAC 180
CTCAAAAACA CTTTGGTGGC CGACTTGATA ATGACACTCA TGCTTCCTTT CAAAATCCTC 240
TCTGACTCAC ACCTGGCACC CTGGCAGCTC AGAGCTTTTG TGTGTCGTTT TTCTTCGGTG 300
15 ATATTTTATG AGACCATGTA TGTGGGCATC GTGCTGTTAG GGCTCATAGC CTTTGACAGA 360
TTCCTCAAGA TCATCAGACC TTTGAGAAAT ATTTTCTAA AAAAACCTGT TTTTGCAAAA 420
ACGGTCTCAA TCTTCATCTG GTTCTTTTGG TTCTTCATCT CCCTGCCAAA TACGATCTTG 480
AGCAACAAGG AAGCAACACC ATCGTCTGTG AAAAAGTGTG CTTCTTTAAA GGGGCCTCTG 540
GGGCTGAAAT GGCATCAAAT GGTAAATAAC ATATGCCAGT TTATTTTCTG GACTGTTTTT 600
20 ATCCTAATGC TTGTGTTTIA TGTGGTTATT GCAAAAAAAG TATATGATTC TTATAGAAAG 660
TCCAAAAGTA AGGACAGAAA AAACAACAAA AAGCTGGAAG GCAAAGTATT TGTGTCGTG 720
GCTGTCTTCT TTGTGTGTTT TGCTCCATTT CATTTTGCCA GAGTTCCATA TACTCACAGT 780
CAAACCAACA ATAAGACTGA CTGTAGACTG CAAAATCAAC TGTTTATTGC TAAAGAAACA 840
ACTCTCTTTT TGGCAGCAAC TAACATTGTG ATGGATCCCT TAATATACAT ATTCTTATGT 900
25 AAAAAATTCA CAGAAAAGCT ACCATGTATG CAAGGGAGAA AGACCACAGC ATCAAGCCAA 960
GAAAATCATA GCAGTCAGAC AGACAACATA ACCTTAGGCT GA 1002

(19) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 333 amino acids
(B) TYPE: amino acid
(C) STRANDEDNESS:

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(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

| | | | | | | | | | | | | | | | | | | | | |
|----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| 5 | Met | Asn | Thr | Thr | Val | Met | Gln | Gly | Phe | Asn | Arg | Ser | Glu | Arg | Cys | Pro | 1 | 5 | 10 | 15 |
| | Arg | Asp | Thr | Arg | Ile | Val | Gln | Leu | Val | Phe | Pro | Ala | Leu | Tyr | Thr | Val | 20 | 25 | 30 | |
| | Val | Phe | Leu | Thr | Gly | Ile | Leu | Leu | Asn | Thr | Leu | Ala | Leu | Trp | Val | Phe | 35 | 40 | 45 | |
| 10 | Val | His | Ile | Pro | Ser | Ser | Ser | Thr | Phe | Ile | Ile | Tyr | Leu | Lys | Asn | Thr | 50 | 55 | 60 | |
| | Leu | Val | Ala | Asp | Leu | Ile | Met | Thr | Leu | Met | Leu | Pro | Phe | Lys | Ile | Leu | 65 | 70 | 75 | 80 |
| 15 | Ser | Asp | Ser | His | Leu | Ala | Pro | Trp | Gln | Leu | Arg | Ala | Phe | Val | Cys | Arg | 85 | 90 | 95 | |
| | Phe | Ser | Ser | Val | Ile | Phe | Tyr | Glu | Thr | Met | Tyr | Val | Gly | Ile | Val | Leu | 100 | 105 | 110 | |
| | Leu | Gly | Leu | Ile | Ala | Phe | Asp | Arg | Phe | Leu | Lys | Ile | Ile | Arg | Pro | Leu | 115 | 120 | 125 | |
| 20 | Arg | Asn | Ile | Phe | Leu | Lys | Lys | Pro | Val | Phe | Ala | Lys | Thr | Val | Ser | Ile | 130 | 135 | 140 | |
| | Phe | Ile | Trp | Phe | Phe | Leu | Phe | Phe | Ile | Ser | Leu | Pro | Asn | Thr | Ile | Leu | 145 | 150 | 155 | 160 |
| 25 | Ser | Asn | Lys | Glu | Ala | Thr | Pro | Ser | Ser | Val | Lys | Lys | Cys | Ala | Ser | Leu | 165 | 170 | 175 | |
| | Lys | Gly | Pro | Leu | Gly | Leu | Lys | Trp | His | Gln | Met | Val | Asn | Asn | Ile | Cys | 180 | 185 | 190 | |
| | Gln | Phe | Ile | Phe | Trp | Thr | Val | Phe | Ile | Leu | Met | Leu | Val | Phe | Tyr | Val | 195 | 200 | 205 | |
| 30 | Val | Ile | Ala | Lys | Lys | Val | Tyr | Asp | Ser | Tyr | Arg | Lys | Ser | Lys | Ser | Lys | 210 | 215 | 220 | |
| | Asp | Arg | Lys | Asn | Asn | Lys | Lys | Leu | Glu | Gly | Lys | Val | Phe | Val | Val | Val | 225 | 230 | 235 | 240 |
| 35 | Ala | Val | Phe | Phe | Val | Cys | Phe | Ala | Pro | Phe | His | Phe | Ala | Arg | Val | Pro | 245 | 250 | 255 | |

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Tyr Thr His Ser Gln Thr Asn Asn Lys Thr Asp Cys Arg Leu Gln Asn
 260 265 270
 Gln Leu Phe Ile Ala Lys Glu Thr Thr Leu Phe Leu Ala Ala Thr Asn
 275 280 285
 5 Ile Cys Met Asp Pro Leu Ile Tyr Ile Phe Leu Cys Lys Lys Phe Thr
 290 295 300
 Glu Lys Leu Pro Cys Met Gln Gly Arg Lys Thr Thr Ala Ser Ser Gln
 305 310 315 320
 10 Glu Asn His Ser Ser Gln Thr Asp Asn Ile Thr Leu Gly
 325 330

(20) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1122 base pairs
 (B) TYPE: nucleic acid
 15 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

ATGGCCAACA CTACCGGAGA GCCTGAGGAG GTGAGCGGCG CTCTGTCCCC ACCGTCCGCA 60
 20 TCAGCTTATG TGAAGCTGGT ACTGCTGGGA CTGATTATGT GCGTGAGCCT GCGGGGTAAC 120
 GCCATCTTGT CCCTGCTGGT GCTCAAGGAG CGTGCCCTGC ACAAGGCTCC TTACTACTTC 180
 CTGCTGGACC TGTGCCTGGC CGATGGCATA CGCTCTGCCG TCTGCTTCCC CTTTGTGCTG 240
 GCTTCTGTGC GCCACGGCTC TTCATGGACC TTCAGTGCAC TCAGCTGCAA GATTGTGGCC 300
 TTTATGGCCG TGCTCTTTTG CTTCCATGCG GCCTTCATGC TGTTCATCAT CAGCGTCACC 360
 25 CGCTACATGG CCATCGCCCA CCACCGCTTC TACGCCAAGC GCATGACACT CTGGACATGC 420
 GCGGCTGTCA TCTGCATGGC CTGGACCCTG TCTGTGGCCA TGGCCTTCCC ACCTGTCTTT 480
 GACGTGGGCA CCTACAAGTT TATTCGGGAG GAGGACCACT GCATCTTTGA GCATCGCTAC 540
 TTCAAGGCCA ATGACACGCT GGGCTTCATG CTTATGTTGG CTGTGCTCAT GGCAGCTACC 600
 CATGCTGTCT ACGGCAAGCT GTCCTCTTC GAGTATCGTC ACCGCAAGAT GAAGCCAGTG 660
 30 CAGATGGTGC CAGCCATCAG CCAGAACTGG ACATTCCATG GTCCCGGGGC CACCGGCCAG 720
 GCTGCTGCCA ACTGGATCGC CGGCTTTGGC CGTGGGCCCA TGCCACCAAC CCTGCTGGGT 780
 ATCCGGCAGA ATGGGCATGC AGCCAGCCGG CGGCTACTGG GCATGGACGA GGTCAAGGGT 840

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GAAAAGCAGC TGGGCCGCAT GTTCTACGCG ATCACACTGC TCTTTCTGCT CCTCTGGTCA 900
 CCCTACATCG TGGCCTGCTA CTGGCGAGTG TTTGTGAAAG CCTGTGCTGT GCCCCACCGC 960
 TACCTGGCCA CTGCTGTTTG GATGAGCTTC GCCCAGGCTG CCGTCAACCC AATTGTCTGC1020
 TTCCTGCTCA ACAAGGACCT CAAGAAGTGC CTGACCACTC ACGCCCCCTG CTGGGGCACA1080
 5 GGAGGTGCCC CGGCTCCCAG AGAACCTAC TGTGTCATGT GA 1122

(21) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 373 amino acids
 (B) TYPE: amino acid
 10 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

15 Met Ala Asn Thr Thr Gly Glu Pro Glu Glu Val Ser Gly Ala Leu Ser
 1 5 10 15
 Pro Pro Ser Ala Ser Ala Tyr Val Lys Leu Val Leu Leu Gly Leu Ile
 20 20 25 30
 Met Cys Val Ser Leu Ala Gly Asn Ala Ile Leu Ser Leu Leu Val Leu
 35 40 45
 20 Lys Glu Arg Ala Leu His Lys Ala Pro Tyr Tyr Phe Leu Leu Asp Leu
 50 55 60
 Cys Leu Ala Asp Gly Ile Arg Ser Ala Val Cys Phe Pro Phe Val Leu
 65 70 75 80
 25 Ala Ser Val Arg His Gly Ser Ser Trp Thr Phe Ser Ala Leu Ser Cys
 85 90 95
 Lys Ile Val Ala Phe Met Ala Val Leu Phe Cys Phe His Ala Ala Phe
 100 105 110
 Met Leu Phe Cys Ile Ser Val Thr Arg Tyr Met Ala Ile Ala His His
 115 120 125
 30 Arg Phe Tyr Ala Lys Arg Met Thr Leu Trp Thr Cys Ala Ala Val Ile
 130 135 140
 Cys Met Ala Trp Thr Leu Ser Val Ala Met Ala Phe Pro Pro Val Phe
 145 150 155 160
 35 Asp Val Gly Thr Tyr Lys Phe Ile Arg Glu Glu Asp Gln Cys Ile Phe
 165 170 175

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Glu His Arg Tyr Phe Lys Ala Asn Asp Thr Leu Gly Phe Met Leu Met
 180 185 190
 Leu Ala Val Leu Met Ala Ala Thr His Ala Val Tyr Gly Lys Leu Leu
 195 200 205
 5 Leu Phe Glu Tyr Arg His Arg Lys Met Lys Pro Val Gln Met Val Pro
 210 215 220
 Ala Ile Ser Gln Asn Trp Thr Phe His Gly Pro Gly Ala Thr Gly Gln
 225 230 235 240
 10 Ala Ala Ala Asn Trp Ile Ala Gly Phe Gly Arg Gly Pro Met Pro Pro
 245 250 255
 Thr Leu Leu Gly Ile Arg Gln Asn Gly His Ala Ala Ser Arg Arg Leu
 260 265 270
 Leu Gly Met Asp Glu Val Lys Gly Glu Lys Gln Leu Gly Arg Met Phe
 275 280 285
 15 Tyr Ala Ile Thr Leu Leu Phe Leu Leu Leu Trp Ser Pro Tyr Ile Val
 290 295 300
 Ala Cys Tyr Trp Arg Val Phe Val Lys Ala Cys Ala Val Pro His Arg
 305 310 315 320
 20 Tyr Leu Ala Thr Ala Val Trp Met Ser Phe Ala Gln Ala Ala Val Asn
 325 330 335
 Pro Ile Val Cys Phe Leu Leu Asn Lys Asp Leu Lys Lys Cys Leu Thr
 340 345 350
 Thr His Ala Pro Cys Trp Gly Thr Gly Gly Ala Pro Ala Pro Arg Glu
 355 360 365
 25 Pro Tyr Cys Val Met
 370

(22) INFORMATION FOR SEQ ID NO:21:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1053 base pairs
 30 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

35 ATGGCTTTGG AACAGAACCA GTCAACAGAT TATTATTATG AGGAAAATGA AATGAATGGC 60
 ACTTATGACT ACAGTCAATA TGAATTGATC TGTATCAAAG AAGATGTCAG AGAATTTGCA 120

AAAGTTTTC TCCCTGTATT CCTCACAATA GCTTTCGTCA TTGGACTTGC AGGCAATTCC 180
 ATGGTAGTGG CAATTTATGC CTATTACAAG AAACAGAGAA CCAAAACAGA TGTGTACATC 240
 CTGAATTTGG CTGTAGCAGA TTTACTCCTT CTATTCACCTC TGCCTTTTGG GGCTGTTAAT 300
 GCAGTTCATG GGTGGGTTTT AGGGAAAATA ATGTGCAAAA TAACTTCAGC CTGTACACA 360
 5 CTAAACTTGG TCTCTGGAAT GCAGTTTCTG GCTTGCATCA GCATAGACAG ATATGTGGCA 420
 GTAACATAATG TCCCCAGCCA ATCAGGAGTG GGAAAACCAT GCTGGATCAT CTGTTTCTGT 480
 GTCTGGATGG CTGCCATCTT GCTGAGCATA CCCCAGCTGG TTTTATATAC AGTAAATGAC 540
 AATGCTAGGT GCATTCCCAT TTTCCCCGC TACCTAGGAA CATCAATGAA AGCATTGATT 600
 CAAATGCTAG AGATCTGCAT TGGATTGTGA GTACCTTTC TTATTATGGG GGTGTGCTAC 660
 10 TTTATCACGG CAAGGACACT CATGAAGATG CCAACATTA AAATATCTCG ACCCCTAAAA 720
 GTTCTGCTCA CAGTCGTTAT AGTTTTCATT GTCACTCAAC TGCCTTATAA CATTGTCAAG 780
 TTCTGCCGAG CCATAGACAT CATCTACTCC CTGATCACCA GCTGCAACAT GAGCAAACGC 840
 ATGGACATCG CCATCCAAGT CACAGAAAGC ATTGCACTCT TTCACAGCTG CCTCAACCCA 900
 ATCCTTTATG TTTTATGGG AGCATCTTC AAAAATACG TTATGAAAGT GGCCAAGAAA 960
 15 TATGGGTCCT GGAGAAGACA GAGACAAAGT GTGGAGGAGT TTCCTTTTGA TTCTGAGGGT 1020
 CCTACAGAGC CAACCAAGTAC TTTTAGCATT TAA 1053

(23) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:

- 20 (A) LENGTH: 350 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

25 Met Ala Leu Glu Gln Asn Gln Ser Thr Asp Tyr Tyr Tyr Glu Glu Asn
 1 5 10 15
 Glu Met Asn Gly Thr Tyr Asp Tyr Ser Gln Tyr Glu Leu Ile Cys Ile
 20 25 30
 30 Lys Glu Asp Val Arg Glu Phe Ala Lys Val Phe Leu Pro Val Phe Leu
 35 40 45
 Thr Ile Ala Phe Val Ile Gly Leu Ala Gly Asn Ser Met Val Val Ala

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| | | | | | |
|----|-----------------------------|---|-----|-----|-----|
| | 50 | | 55 | | 60 |
| | Ile Tyr Ala Tyr Tyr | Lys Lys Gln Arg Thr Lys Thr Asp Val Tyr Ile | | | |
| | 65 | 70 | 75 | 80 | |
| 5 | Leu Asn Leu Ala Val | Ala Asp Leu Leu Leu Phe Thr Leu Pro Phe | | | |
| | | 85 | 90 | 95 | |
| | Trp Ala Val Asn Ala Val | His Gly Trp Val Leu Gly Lys Ile Met Cys | | | |
| | | 100 | 105 | 110 | |
| | Lys Ile Thr Ser Ala Leu Tyr | Thr Leu Asn Phe Val Ser Gly Met Gln | | | |
| | | 115 | 120 | 125 | |
| 10 | Phe Leu Ala Cys Ile Ser | Ile Asp Arg Tyr Val Ala Val Thr Asn Val | | | |
| | | 130 | 135 | 140 | |
| | Pro Ser Gln Ser Gly Val | Gly Lys Pro Cys Trp Ile Ile Cys Phe Cys | | | |
| | | 145 | 150 | 155 | 160 |
| 15 | Val Trp Met Ala Ala | Ile Leu Leu Ser Ile Pro Gln Leu Val Phe Tyr | | | |
| | | 165 | 170 | 175 | |
| | Thr Val Asn Asp Asn Ala | Arg Cys Ile Pro Ile Phe Pro Arg Tyr Leu | | | |
| | | 180 | 185 | 190 | |
| | Gly Thr Ser Met Lys Ala | Leu Ile Gln Met Leu Glu Ile Cys Ile Gly | | | |
| | | 195 | 200 | 205 | |
| 20 | Phe Val Val Pro Phe Leu | Ile Met Gly Val Cys Tyr Phe Ile Thr Ala | | | |
| | | 210 | 215 | 220 | |
| | Arg Thr Leu Met Lys Met | Pro Asn Ile Lys Ile Ser Arg Pro Leu Lys | | | |
| | | 225 | 230 | 235 | 240 |
| 25 | Val Leu Leu Thr Val Val | Ile Val Phe Ile Val Thr Gln Leu Pro Tyr | | | |
| | | 245 | 250 | 255 | |
| | Asn Ile Val Lys Phe Cys | Arg Ala Ile Asp Ile Ile Tyr Ser Leu Ile | | | |
| | | 260 | 265 | 270 | |
| | Thr Ser Cys Asn Met Ser | Lys Arg Met Asp Ile Ala Ile Gln Val Thr | | | |
| | | 275 | 280 | 285 | |
| 30 | Glu Ser Ile Ala Leu Phe | His Ser Cys Leu Asn Pro Ile Leu Tyr Val | | | |
| | | 290 | 295 | 300 | |
| | Phe Met Gly Ala Ser Phe | Lys Asn Tyr Val Met Lys Val Ala Lys Lys | | | |
| | | 305 | 310 | 315 | 320 |
| 35 | Tyr Gly Ser Trp Arg Arg | Gln Arg Gln Ser Val Glu Glu Phe Pro Phe | | | |
| | | 325 | 330 | 335 | |
| | Asp Ser Glu Gly Pro Thr | Glu Pro Thr Ser Thr Phe Ser Ile | | | |
| | | 340 | 345 | 350 | |

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(24) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 1116 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

ATGCCAGGAA ACGCCACCCC AGTGACCACC ACTGCCCCGT GGGCCTCCCT GGGCCTCTCC 60
10 GCCAAGACCT GCAACAACGT GTCCTTCGAA GAGAGCAGGA TAGTCCTGGT CGTGGTGTAC 120
AGCGCGGTGT GCACGCTGGG GGTGCCGGCC AACTGCCTGA CTGCGTGGCT GGCCTGCTG 180
CAGGTACTGC AGGGCAACGT GCTGGCCGTC TACCTGCTCT GCCTGGCACT CTGCGAACTG 240
CTGTACACAG GCACGCTGCC ACTCTGGGTC ATCTATATCC GCAACCAGCA CCGCTGGACC 300
CTAGGCCTGC TGGCCTCGAA GGTGACCGCC TACATCTTCT TCTGCAACAT CTACGTCAGC 360
15 ATCCTCTTCC TGTGCTGCAT CTCCTGCGAC CGCTTCGTGG CCGTGGTGTG CGCGCTGGAG 420
AGTCGGGGCC GCCGCCGCCG GAGGACCGCC ATCCTCATCT CCGCCTGCAT CTTTCATCTC 480
GTCGGGATCG TTCCTACCC GGTGTTCCAG ACGGAAGACA AGGAGACCTG CTTTGACATG 540
CTGCAGATGG ACAGCAGGAT TGCCGGGTAC TACTACGCCA GGTTCACCGT TGGCTTTGCC 600
ATCCCTCTCT CCATCATCGC CTTACCAAC CACCGGATT TTAGGAGCAT CAAGCAGAGC 660
20 ATGGGCTTAA GCGCTGCCCA GAAGGCCAAG GTGAAGCACT CGGCCATCGC GGTGGTTGTC 720
ATCTTCCTAG TCTGCTTCGC CCCGTACCAC CTGGTTCTCC TCGTCAAAGC CGCTGCCTTT 780
TCCTACTACA GAGGAGACAG GAACGCCATG TGCGGCTTGG AGGAAAGGCT GTACACAGCC 840
TCTGTGGTGT TTCTGTGCCT GTCCACGGTG AACGGCGTGG CTGACCCCAT TATCTACGTG 900
CTGGCCACGG ACCATTCCCG CCAAGAAGTG TCCAGAATCC ATAAGGGGTG GAAAGAGTGG 960
25 TCCATGAAGA CAGACGTCAC CAGGCTCACC CACAGCAGGG ACACCGAGGA GCTGCAGTCG1020
CCCGTGGCCC TTGACAGACCA CTACACCTTC TCCAGGCCCG TGCACCCACC AGGGTCACCA1080
TGCCCTGCAA AGAGGCTGAT TGAGGAGTCC TGCTGA 1116

(25) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:

- 30 (A) LENGTH: 371 amino acids

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- (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

```

Met Pro Gly Asn Ala Thr Pro Val Thr Thr Thr Ala Pro Trp Ala Ser
1           5           10           15

Leu Gly Leu Ser Ala Lys Thr Cys Asn Asn Val Ser Phe Glu Glu Ser
          20           25           30

10 Arg Ile Val Leu Val Val Val Tyr Ser Ala Val Cys Thr Leu Gly Val
    35           40           45

Pro Ala Asn Cys Leu Thr Ala Trp Leu Ala Leu Leu Gln Val Leu Gln
    50           55           60

15 Gly Asn Val Leu Ala Val Tyr Leu Leu Cys Leu Ala Leu Cys Glu Leu
    65           70           75           80

Leu Tyr Thr Gly Thr Leu Pro Leu Trp Val Ile Tyr Ile Arg Asn Gln
          85           90           95

His Arg Trp Thr Leu Gly Leu Leu Ala Ser Lys Val Thr Ala Tyr Ile
          100          105          110

20 Phe Phe Cys Asn Ile Tyr Val Ser Ile Leu Phe Leu Cys Cys Ile Ser
    115           120           125

Cys Asp Arg Phe Val Ala Val Val Tyr Ala Leu Glu Ser Arg Gly Arg
    130           135           140

25 Arg Arg Arg Arg Thr Ala Ile Leu Ile Ser Ala Cys Ile Phe Ile Leu
    145           150           155           160

Val Gly Ile Val His Tyr Pro Val Phe Gln Thr Glu Asp Lys Glu Thr
          165           170           175

Cys Phe Asp Met Leu Gln Met Asp Ser Arg Ile Ala Gly Tyr Tyr Tyr
          180           185           190

30 Ala Arg Phe Thr Val Gly Phe Ala Ile Pro Leu Ser Ile Ile Ala Phe
    195           200           205

Thr Asn His Arg Ile Phe Arg Ser Ile Lys Gln Ser Met Gly Leu Ser
    210           215           220

35 Ala Ala Gln Lys Ala Lys Val Lys His Ser Ala Ile Ala Val Val Val
    225           230           235           240
  
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Ile Phe Leu Val Cys Phe Ala Pro Tyr His Leu Val Leu Leu Val Lys
 245 250 255

Ala Ala Ala Phe Ser Tyr Tyr Arg Gly Asp Arg Asn Ala Met Cys Gly
 260 265 270

5 Leu Glu Glu Arg Leu Tyr Thr Ala Ser Val Val Phe Leu Cys Leu Ser
 275 280 285

Thr Val Asn Gly Val Ala Asp Pro Ile Ile Tyr Val Leu Ala Thr Asp
 290 295 300

10 His Ser Arg Gln Glu Val Ser Arg Ile His Lys Gly Trp Lys Glu Trp
 305 310 315 320

Ser Met Lys Thr Asp Val Thr Arg Leu Thr His Ser Arg Asp Thr Glu
 325 330 335

Glu Leu Gln Ser Pro Val Ala Leu Ala Asp His Tyr Thr Phe Ser Arg
 340 345 350

15 Pro Val His Pro Pro Gly Ser Pro Cys Pro Ala Lys Arg Leu Ile Glu
 355 360 365

Glu Ser Cys
 370

(26) INFORMATION FOR SEQ ID NO:25:

- 20 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 1113 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- 25 (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

ATGGCGAACT ATAGCCATGC AGCTGACAAC ATTTTGCAAA ATCTCTCGCC TCTAACAGCC 60
 TTTCTGAAAC TGAATTCCTT GGGTTTCATA ATAGGAGTCA GCGTGGTGGG CAACCTCCTG 120
 ATCTCCATTT TGCTAGTGAA AGATAAGACC TTGCATAGAG CACCTTACTA CTTCTGTGTTG 180
 30 GATCTTTGCT GTTCAGATAT CCTCAGATCT GCAATTTGTT TCCCATTTGT GTTCAACTCT 240
 GTCAAAAATG GCTCTACCTG GACTTATGGG ACTCTGACTT GCAAAGTGAT TGCCTTTCTG 300
 GGGGTTTTGT CCTGTTTCCA CACTGCTTTC ATGCTCTTCT GCATCAGTGT CACCAGATAC 360
 TTAGCTATCG CCCATCACCG CTTCTATACA AAGAGGCTGA CCTTTTGGAC GTGTCTGGCT 420
 GTGATCTGTA TGGTGTGGAC TCTGTCTGTG GCCATGGCAT TTCCCCCGGT TTTAGACGTG 480

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GGCACCTTACT CATTTCATTAG GGAGGAAGAT CAATGCACCT TCCAACACCG CTCCTTCAGG 540
 GCTAATGATT CCTTAGGATT TATGCTGCTT CTTGCTCTCA TCCTCCTAGC CACACAGCTT 600
 GTCTACCTCA AGCTGATATT TTTCGTCCAC GATCGAAGAA AAATGAAGCC AGTCCAGTTT 660
 GTAGCAGCAG TCAGCCAGAA CTGGACTTTT CATGGTCCTG GAGCCAGTGG CCAGGCAGCT 720
 5 GCCAATTGGC TAGCAGGATT TGAAGGGGT CCCACACCAC CCACCTTGCT GGGCATCAGG 780
 CAAATGCAA ACACCACAGG CAGAAGAAGG CTATTGGTCT TAGACGAGTT CAAATGGAG 840
 AAAAGAATCA GCAGAATGTT CTATATAATG ACTTTTCTGT TTCTAACCTT GTGGGGCCCC 900
 TACCTGGTGG CCTGTTATTG GAGAGTTTTT GCAAGAGGGC CTGTAGTACC AGGGGGATT 960
 CTAACAGCTG CTGTCTGGAT GAGTTTTGCC CAAGCAGGAA TCAATCCTTT TGTCTGCATT 1020
 10 TTCTCAAACA GGGAGCTGAG GCGCTGTTTC AGCACAACCC TTCTTTACTG CAGAAAATCC 1080
 AGGTTACCAA GGAACCTTA CTGTGTTATA TGA 1113

(27) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 370 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

20 Met Ala Asn Tyr Ser His Ala Ala Asp Asn Ile Leu Gln Asn Leu Ser
 1 5 10 15
 Pro Leu Thr Ala Phe Leu Lys Leu Thr Ser Leu Gly Phe Ile Ile Gly
 20 25 30
 25 Val Ser Val Val Gly Asn Leu Leu Ile Ser Ile Leu Leu Val Lys Asp
 35 40 45
 Lys Thr Leu His Arg Ala Pro Tyr Tyr Phe Leu Leu Asp Leu Cys Cys
 50 55 60
 Ser Asp Ile Leu Arg Ser Ala Ile Cys Phe Pro Phe Val Phe Asn Ser
 65 70 75 80
 30 Val Lys Asn Gly Ser Thr Trp Thr Tyr Gly Thr Leu Thr Cys Lys Val
 85 90 95
 Ile Ala Phe Leu Gly Val Leu Ser Cys Phe His Thr Ala Phe Met Leu

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| | 100 | 105 | 110 |
|----|---|---------|---------|
| | Phe Cys Ile Ser Val Thr Arg Tyr Leu Ala Ile Ala His His Arg Phe | | |
| | 115 | 120 | 125 |
| 5 | Tyr Thr Lys Arg Leu Thr Phe Trp Thr Cys Leu Ala Val Ile Cys Met | | |
| | 130 | 135 | 140 |
| | Val Trp Thr Leu Ser Val Ala Met Ala Phe Pro Pro Val Leu Asp Val | | |
| | 145 | 150 | 155 160 |
| | Gly Thr Tyr Ser Phe Ile Arg Glu Glu Asp Gln Cys Thr Phe Gln His | | |
| | | 165 170 | 175 |
| 10 | Arg Ser Phe Arg Ala Asn Asp Ser Leu Gly Phe Met Leu Leu Leu Ala | | |
| | | 180 185 | 190 |
| | Leu Ile Leu Leu Ala Thr Gln Leu Val Tyr Leu Lys Leu Ile Phe Phe | | |
| | | 195 200 | 205 |
| 15 | Val His Asp Arg Arg Lys Met Lys Pro Val Gln Phe Val Ala Ala Val | | |
| | | 210 215 | 220 |
| | Ser Gln Asn Trp Thr Phe His Gly Pro Gly Ala Ser Gly Gln Ala Ala | | |
| | | 225 230 | 235 240 |
| | Ala Asn Trp Leu Ala Gly Phe Gly Arg Gly Pro Thr Pro Pro Thr Leu | | |
| | | 245 250 | 255 |
| 20 | Leu Gly Ile Arg Gln Asn Ala Asn Thr Thr Gly Arg Arg Arg Leu Leu | | |
| | | 260 265 | 270 |
| | Val Leu Asp Glu Phe Lys Met Glu Lys Arg Ile Ser Arg Met Phe Tyr | | |
| | | 275 280 | 285 |
| 25 | Ile Met Thr Phe Leu Phe Leu Thr Leu Trp Gly Pro Tyr Leu Val Ala | | |
| | | 290 295 | 300 |
| | Cys Tyr Trp Arg Val Phe Ala Arg Gly Pro Val Val Pro Gly Gly Phe | | |
| | | 305 310 | 315 320 |
| | Leu Thr Ala Ala Val Trp Met Ser Phe Ala Gln Ala Gly Ile Asn Pro | | |
| | | 325 330 | 335 |
| 30 | Phe Val Cys Ile Phe Ser Asn Arg Glu Leu Arg Arg Cys Phe Ser Thr | | |
| | | 340 345 | 350 |
| | Thr Leu Leu Tyr Cys Arg Lys Ser Arg Leu Pro Arg Glu Pro Tyr Cys | | |
| | | 355 360 | 365 |
| 35 | Val Ile | | |
| | 370 | | |

(28) INFORMATION FOR SEQ ID NO:27:

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(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1080 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
5 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

ATGCAGGTCC CGAACAGCAC CGGCCCGGAC AACGCGACGC TGCAGATGCT GCGGAACCCG 60
GCGATCGCGG TGGCCCTGCC CGTGGTGTAC TCGCTGGTGG CGGCGGTCTAG CATCCCGGGC 120
10 AACCTCTTCT CTCTGTGGGT GCTGTGCCGG CGCATGGGGC CCAGATCCCC GTCGGTCATC 180
TTCATGATCA ACCTGAGCGT CACGGACCTG ATGCTGGCCA GCGTGTGCC TTTCCAAATC 240
TACTACCATT GCAACCGCCA CCACTGGGTA TTCGGGGTGC TGCTTTGCAA CGTGGTGACC 300
GTGGCCTTTT ACGCAAACAT GTATTCCAGC ATCCTCACCA TGACCTGTAT CAGCGTGGAG 360
CGCTTCCTGG GGGTCCTGTA CCCGCTCAGC TCCAAGCGCT GGCGCCGCCG TCGTTACGCG 420
15 GTGGCCGCGT GTGCAGGGAC CTGGCTGCTG CTCCTGACCG CCCTGTGCCC GCTGGCGCGC 480
ACCGATCTCA CCTACCCGGT GCACGCCCTG GGCATCATCA CCTGCTTCGA CGTCCTCAAG 540
TGGACGATGC TCCCCAGCGT GGCCATGTGG GCCGTGTTCC TCCTCACCAT CTTTCATCCTG 600
CTGTTCTCTA TCCCGTTCGT GATCACCGTG GCTTGTTACA CGGCCACCAT CCTCAAGCTG 660
TTGCGCACGG AGGAGGCGCA CGGCCGGGAG CAGCGGAGGC GCGCGGTGGG CCTGGCCGCG 720
20 GTGGTCTTGC TGGCCTTTGT CACCTGCTTC GCCCCCAACA ACTTCGTGCT CCTGGCGCAC 780
ATCGTGAGCC GCCTGTTCTA CGGCAAGAGC TACTACCACG TGTACAAGCT CACGCTGTGT 840
CTCAGCTGCC TCAACAACTG TCTGGACCCG TTTGTTTATT ACTTTGCGTC CCGGAATTC 900
CAGCTGCGCC TGCGGGAATA TTTGGGCTGC CGCCGGGTGC CCAGAGACAC CCTGGACACG 960
CGCCGCGAGA GCCTCTTCTC CGCCAGGACC ACGTCCGTGC GCTCCGAGGC CGGTGCGCAC1020
25 CCTGAAGGGA TGGAGGGAGC CACCAGGCCC GGCCTCCAGA GGCAGGAGAG TGTGTTCTGA1080

(29) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 359 amino acids
(B) TYPE: amino acid
30 (C) STRANDEDNESS:
(D) TOPOLOGY: not relevant

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(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

```

Met Gln Val Pro Asn Ser Thr Gly Pro Asp Asn Ala Thr Leu Gln Met
1           5           10           15
5  Leu Arg Asn Pro Ala Ile Ala Val Ala Leu Pro Val Val Tyr Ser Leu
    20           25           30
Val Ala Ala Val Ser Ile Pro Gly Asn Leu Phe Ser Leu Trp Val Leu
    35           40           45
10 Cys Arg Arg Met Gly Pro Arg Ser Pro Ser Val Ile Phe Met Ile Asn
    50           55           60
Leu Ser Val Thr Asp Leu Met Leu Ala Ser Val Leu Pro Phe Gln Ile
    65           70           75           80
Tyr Tyr His Cys Asn Arg His His Trp Val Phe Gly Val Leu Leu Cys
    85           90           95
15 Asn Val Val Thr Val Ala Phe Tyr Ala Asn Met Tyr Ser Ser Ile Leu
    100          105          110
Thr Met Thr Cys Ile Ser Val Glu Arg Phe Leu Gly Val Leu Tyr Pro
    115          120          125
20 Leu Ser Ser Lys Arg Trp Arg Arg Arg Arg Tyr Ala Val Ala Ala Cys
    130          135          140
Ala Gly Thr Trp Leu Leu Leu Leu Thr Ala Leu Cys Pro Leu Ala Arg
    145          150          155          160
Thr Asp Leu Thr Tyr Pro Val His Ala Leu Gly Ile Ile Thr Cys Phe
    165          170          175
25 Asp Val Leu Lys Trp Thr Met Leu Pro Ser Val Ala Met Trp Ala Val
    180          185          190
Phe Leu Phe Thr Ile Phe Ile Leu Leu Phe Leu Ile Pro Phe Val Ile
    195          200          205
30 Thr Val Ala Cys Tyr Thr Ala Thr Ile Leu Lys Leu Leu Arg Thr Glu
    210          215          220
Glu Ala His Gly Arg Glu Gln Arg Arg Arg Ala Val Gly Leu Ala Ala
    225          230          235          240
Val Val Leu Leu Ala Phe Val Thr Cys Phe Ala Pro Asn Asn Phe Val
    245          250          255
35 Leu Leu Ala His Ile Val Ser Arg Leu Phe Tyr Gly Lys Ser Tyr Tyr
    260          265          270

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His Val Tyr Lys Leu Thr Leu Cys Leu Ser Cys Leu Asn Asn Cys Leu
 275 280 285

Asp Pro Phe Val Tyr Tyr Phe Ala Ser Arg Glu Phe Gln Leu Arg Leu
 290 295 300

5 Arg Glu Tyr Leu Gly Cys Arg Arg Val Pro Arg Asp Thr Leu Asp Thr
 305 310 315 320

Arg Arg Glu Ser Leu Phe Ser Ala Arg Thr Thr Ser Val Arg Ser Glu
 325 330 335

10 Ala Gly Ala His Pro Glu Gly Met Glu Gly Ala Thr Arg Pro Gly Leu
 340 345 350

Gln Arg Gln Glu Ser Val Phe
 355

(30) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 1503 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

ATGGAGCGTC CCTGGGAGGA CAGCCCAGGC CCGGAGGGGG CAGCTGAGGG CTCGCCTGTG 60

CCAGTCGCCG CCGGGGCGCG CTCGGGTGCC GCGGCGAGTG GCACAGGCTG GCAGCCATGG 120

GCTGAGTGCC CGGGACCCAA GGGGAGGGGG CAACTGCTGG CGACCGCCGG CCTTTGCGT 180

CGCTGGCCCG CCCCTCGCC TGCCAGCTCC AGCCCCGCCC CCGGAGCGGC GTCCGCTCAC 240

25 TCGGTTCAAG GCAGCGCGAC TGCGGGTGGC GCACGACCAG GGCGCAGACC TTGGGGCGCG 300

CGGCCCATGG AGTCGGGGCT GCTGCGGCCG GCGCCGGTGA GCGAGGTCAT CGTCCTGCAT 360

TACAACTACA CCGGCAAGCT CCGCGGTGCG AGCTACCAGC CGGGTGCCGG CCTGCGCGCC 420

GACGCCGTGG TGTGCCTGGC GGTGTGCGCC TTCATCGTGC TAGAGAATCT AGCCGTGTTG 480

TTGGTGCTCG GACGCCACCC GCGCTTCCAC GCTCCCATGT TCCTGCTCCT GGGCAGCCTC 540

30 ACGTTGTGCG ATCTGCTGGC AGGCGCCGCC TACGCCGCCA ACATCCTACT GTCGGGGCCG 600

CTCACGCTGA AACTGTCCCC CGCGCTCTGG TTGCGACGGG AGGGAGGCGT CTTGCTGGCA 660

CTCACTGCGT CCGTGCTGAG CCTCCTGGCC ATCGCGCTGG AGCGCAGCCT CACCATGGCG 720

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CGCAGGGGGC CCGCGCCCGT CTCCAGTCGG GGGCGCACGC TGGCGATGGC AGCCGCGGCC 780
 TGGGGCGTGT CGCTGCTCCT CGGGCTCCTG CCAGCGCTGG GCTGGAATTG CCTGGGTCGC 840
 CTGGACGCTT GCTCCACTGT CTTGCCGCTC TACGCCAAGG CCTACGTGCT CTTCTGEGTG 900
 CTCGCCTTCG TGGGCATCCT GGCCGCGATC TGTGCACTCT ACGCGCGCAT CTA CTGCCAG 960
 5 GTACGCGCCA ACGCGCGGCG CTGCGCGGCA CGGCCCCGGA CTGCGGGGAC CACCTCGACC1020
 CGGGCGCGTC GCAAGCCGCG CTCTCTGGCC TTGCTGCGCA CGCTCAGCGT GGTGCTCCTG1080
 GCCTTTGTGG CATGTTGGGG CCCCCTCTTC CTGCTGCTGT TGCTCGACGT GGCCTGCCCCG1140
 GCGCGCACCT GTCCTGTACT CCTGCAGGCC GATCCCTTCC TGGGACTGGC CATGGCCAAC1200
 TCACTTCTGA ACCCATCAT CTACACGCTC ACCAACCGCG ACCTGCGCCA CGCGCTCCTG1260
 10 CGCCTGGTCT GCTGCGGACG CCACTCCTGC GGCAGAGACC CGAGTGGCTC CCAGCAGTCG1320
 GCGAGCGCGG CTGAGGCTTC CGGGGGCCTG CGCCGCTGCC TGCCCCCGGG CCTTGATGGG1380
 AGCTTCAGCG GCTCGGAGCG CTCATCGCCC CAGCGCGACG GGCTGGACAC CAGCGGCTCC1440
 ACAGGCAGCC CCGGTGCACC CACAGCCGCC CGGACTCTGG TATCAGAACC GGCTGCAGAC1500
 TGA 1503

15 (31) INFORMATION FOR SEQ ID NO:30:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 500 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 20 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Met Glu Arg Pro Trp Glu Asp Ser Pro Gly Pro Glu Gly Ala Ala Glu
 1 5 10 15
 25 Gly Ser Pro Val Pro Val Ala Ala Gly Ala Arg Ser Gly Ala Ala Ala
 20 25 30
 Ser Gly Thr Gly Trp Gln Pro Trp Ala Glu Cys Pro Gly Pro Lys Gly
 35 40 45
 30 Arg Gly Gln Leu Leu Ala Thr Ala Gly Pro Leu Arg Arg Trp Pro Ala
 50 55 60
 Pro Ser Pro Ala Ser Ser Ser Pro Ala Pro Gly Ala Ala Ser Ala His
 65 70 75 80

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Ser Val Gln Gly Ser Ala Thr Ala Gly Gly Ala Arg Pro Gly Arg Arg
 85 90 95
 Pro Trp Gly Ala Arg Pro Met Glu Ser Gly Leu Leu Arg Pro Ala Pro
 100 105 110
 5 Val Ser Glu Val Ile Val Leu His Tyr Asn Tyr Thr Gly Lys Leu Arg
 115 120 125
 Gly Ala Ser Tyr Gln Pro Gly Ala Gly Leu Arg Ala Asp Ala Val Val
 130 135 140
 10 Cys Leu Ala Val Cys Ala Phe Ile Val Leu Glu Asn Leu Ala Val Leu
 145 150 155 160
 Leu Val Leu Gly Arg His Pro Arg Phe His Ala Pro Met Phe Leu Leu
 165 170 175
 Leu Gly Ser Leu Thr Leu Ser Asp Leu Leu Ala Gly Ala Ala Tyr Ala
 180 185 190
 15 Ala Asn Ile Leu Leu Ser Gly Pro Leu Thr Leu Lys Leu Ser Pro Ala
 195 200 205
 Leu Trp Phe Ala Arg Glu Gly Gly Val Phe Val Ala Leu Thr Ala Ser
 210 215 220
 20 Val Leu Ser Leu Leu Ala Ile Ala Leu Glu Arg Ser Leu Thr Met Ala
 225 230 235 240
 Arg Arg Gly Pro Ala Pro Val Ser Ser Arg Gly Arg Thr Leu Ala Met
 245 250 255
 Ala Ala Ala Ala Trp Gly Val Ser Leu Leu Leu Gly Leu Leu Pro Ala
 260 265 270
 25 Leu Gly Trp Asn Cys Leu Gly Arg Leu Asp Ala Cys Ser Thr Val Leu
 275 280 285
 Pro Leu Tyr Ala Lys Ala Tyr Val Leu Phe Cys Val Leu Ala Phe Val
 290 295 300
 30 Gly Ile Leu Ala Ala Ile Cys Ala Leu Tyr Ala Arg Ile Tyr Cys Gln
 305 310 315 320
 Val Arg Ala Asn Ala Arg Arg Leu Pro Ala Arg Pro Gly Thr Ala Gly
 325 330 335
 Thr Thr Ser Thr Arg Ala Arg Arg Lys Pro Arg Ser Leu Ala Leu Leu
 340 345 350
 35 Arg Thr Leu Ser Val Val Leu Leu Ala Phe Val Ala Cys Trp Gly Pro
 355 360 365
 Leu Phe Leu Leu Leu Leu Leu Asp Val Ala Cys Pro Ala Arg Thr Cys

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| | | | | | |
|----|---|-----|-----|-----|---------|
| | 370 | | 375 | | 380 |
| | Pro Val Leu Leu Gln Ala Asp Pro Phe Leu Gly Leu Ala Met Ala Asn | | | | |
| | 385 | | 390 | | 395 400 |
| 5 | Ser Leu Leu Asn Pro Ile Ile Tyr Thr Leu Thr Asn Arg Asp Leu Arg | | | | |
| | | 405 | | 410 | 415 |
| | His Ala Leu Leu Arg Leu Val Cys Cys Gly Arg His Ser Cys Gly Arg | | | | |
| | | 420 | 425 | | 430 |
| | Asp Pro Ser Gly Ser Gln Gln Ser Ala Ser Ala Ala Glu Ala Ser Gly | | | | |
| | | 435 | 440 | | 445 |
| 10 | Gly Leu Arg Arg Cys Leu Pro Pro Gly Leu Asp Gly Ser Phe Ser Gly | | | | |
| | | 450 | 455 | | 460 |
| | Ser Glu Arg Ser Ser Pro Gln Arg Asp Gly Leu Asp Thr Ser Gly Ser | | | | |
| | | 465 | 470 | 475 | 480 |
| 15 | Thr Gly Ser Pro Gly Ala Pro Thr Ala Ala Arg Thr Leu Val Ser Glu | | | | |
| | | 485 | 490 | | 495 |
| | Pro Ala Ala Asp | | | | |
| | | 500 | | | |

(32) INFORMATION FOR SEQ ID NO:31:

- (i) SEQUENCE CHARACTERISTICS:
- 20 (A) LENGTH: 1029 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

ATGCAAGCCG TCGACAATCT CACCTCTGCG CCTGGGAACA CCAGTCTGTG CACCAGAGAC 60

TACAAAATCA CCCAGGTCCT CTCCCACTG CTCTACACTG TCCTGTTTTT TGTGGACTT 120

ATCACAAATG GCCTGGCGAT GAGGATTTTC TTCAAATCC GGAGTAAATC AAACCTTTATT 180

ATTTTTCTTA AGAACACAGT CATTTCTGAT CTCTCATGA TTCTGACTTT TCCATTCAAA 240

30 ATTCTTAGTG ATGCCAAACT GGAACAGGA CCACTGAGAA CTTTGTGTG TCAAGTTACC 300

TCCGTCATAT TTTATTTCAC AATGTATATC AGTATTTTCT TCCTGGGACT GATAACTATC 360

GATCGCTACC AGAAGACCAC CAGGCCATTT AAAACATCCA ACCCCAAAAA TCTCTTGGGG 420

GCTAAGATTC TCTCTGTTGT CATCTGGGCA TTCATGTTCT TACTCTCTTT GCCTAACATG 480

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ATTCTGACCA ACAGGCAGCC GAGAGACAAG AATGTGAAGA AATGCTCTTT CCTTAAATCA 540
 GAGTTCGGTC TAGTCTGGCA TGAAATAGTA AATTACATCT GTCAAGTCAT TTTCTGGATT 600
 AATTTCTTAA TTGTTATTGT ATGTTATACA CTCATTACAA AAGAACTGTA CCGGTCATAC 660
 GTAAGAACGA GGGGTGTAGG TAAAGTCCCC AGGAAAAAGG TGAACGTCAA AGTTTTTCATT 720
 5 ATCATTGCTG TATTCTTTAT TTGTTTGT TCTTCCATT TTGCCC GAAT TCCTTACACC 780
 CTGAGCCAAA CCCGGGATGT CTTTGACTGC ACTGCTGAAA ATACTCTGTT CTATGTGAAA 840
 GAGAGCACTC TGTGGTTAAC TTCCTTAAAT GCATGCCTGG ATCCGTTTCAT CTATTTTTTC 900
 CTTTGCAAGT CCTTCAGAAA TTCCTTGATA AGTATGCTGA AGTGCCCCAA TTCTGCAACA 960
 TCTCTGTCCC AGGACAATAG GAAAAAGAA CAGGATGGTG GTGACCCAAA TGAAGAGACT 1020
 10 CCAATGTAA 1029

(33) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 342 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

20 Met Gln Ala Val Asp Asn Leu Thr Ser Ala Pro Gly Asn Thr Ser Leu
 1 5 10 15
 Cys Thr Arg Asp Tyr Lys Ile Thr Gln Val Leu Phe Pro Leu Leu Tyr
 20 25 30
 Thr Val Leu Phe Phe Val Gly Leu Ile Thr Asn Gly Leu Ala Met Arg
 35 40 45
 25 Ile Phe Phe Gln Ile Arg Ser Lys Ser Asn Phe Ile Ile Phe Leu Lys
 50 55 60
 Asn Thr Val Ile Ser Asp Leu Leu Met Ile Leu Thr Phe Pro Phe Lys
 65 70 75 80
 30 Ile Leu Ser Asp Ala Lys Leu Gly Thr Gly Pro Leu Arg Thr Phe Val
 85 90 95
 Cys Gln Val Thr Ser Val Ile Phe Tyr Phe Thr Met Tyr Ile Ser Ile
 100 105 110
 Ser Phe Leu Gly Leu Ile Thr Ile Asp Arg Tyr Gln Lys Thr Thr Arg

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| | | | |
|----|---|---|-------------|
| | 115 | 120 | 125 |
| | Pro Phe Lys Thr Ser Asn | Pro Lys Asn Leu Leu Gly Ala Lys Ile Leu | |
| | 130 | 135 | 140 |
| 5 | Ser Val Val Ile Trp Ala Phe Met Phe Leu Leu Ser Leu Pro Asn Met | | |
| | 145 | 150 | 155 160 |
| | Ile Leu Thr Asn Arg Gln Pro Arg Asp Lys Asn Val Lys Lys Cys Ser | | |
| | | 165 | 170 175 |
| | Phe Leu Lys Ser Glu Phe Gly Leu Val Trp His Glu Ile Val Asn Tyr | | |
| | | 180 | 185 190 |
| 10 | Ile Cys Gln Val Ile Phe Trp Ile Asn Phe Leu Ile Val Ile Val Cys | | |
| | | 195 | 200 205 |
| | Tyr Thr Leu Ile Thr Lys Glu Leu Tyr Arg Ser Tyr Val Arg Thr Arg | | |
| | | 210 | 215 220 |
| 15 | Gly Val Gly Lys Val Pro Arg Lys Lys Val Asn Val Lys Val Phe Ile | | |
| | | 225 | 230 235 240 |
| | Ile Ile Ala Val Phe Phe Ile Cys Phe Val Pro Phe His Phe Ala Arg | | |
| | | 245 | 250 255 |
| | Ile Pro Tyr Thr Leu Ser Gln Thr Arg Asp Val Phe Asp Cys Thr Ala | | |
| | | 260 | 265 270 |
| 20 | Glu Asn Thr Leu Phe Tyr Val Lys Glu Ser Thr Leu Trp Leu Thr Ser | | |
| | | 275 | 280 285 |
| | Leu Asn Ala Cys Leu Asp Pro Phe Ile Tyr Phe Phe Leu Cys Lys Ser | | |
| | | 290 | 295 300 |
| 25 | Phe Arg Asn Ser Leu Ile Ser Met Leu Lys Cys Pro Asn Ser Ala Thr | | |
| | | 305 | 310 315 320 |
| | Ser Leu Ser Gln Asp Asn Arg Lys Lys Glu Gln Asp Gly Gly Asp Pro | | |
| | | 325 | 330 335 |
| | Asn Glu Glu Thr Pro Met | | |
| | | 340 | |

30 (34) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1077 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

35 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

ATGTCGGTCT GCTACCGTCC CCCAGGGAAC GAGACACTGC TGAGCTGGAA GACTTCGCGG 60
 GCCACAGGCA CAGCCTTCCT GCTGCTGGCG GCGCTGCTGG GGCTGCCTGG CAACGGCTTC 120
 TGGTGTGGA GCTTGGCGGG CTGGCGGCCT GCACGGGGGC GACCGCTGGC GGCCACGCTT 180
 5 GTGCTGCACC TGGCGCTGGC CGACGGCGCG GTGCTGCTGC TCACGCCGCT CTTTGTGGCC 240
 TTCCTGACCC GGCAGGCCTG GCCGCTGGGC CAGGCGGGCT GCAAGGCGGT GTACTACGTG 300
 TGCGCGCTCA GCATGTACGC CAGCGTGCTG CTCACCGGCC TGCTCAGCCT GCAGCGCTGC 360
 CTCGCACTCA CCCGCCCTT CCTGGCGCCT CGGCTGCGCA GCGCGGCCCT GGCCCGCCGC 420
 CTGCTGCTGG CGTCTGGCT GGCGCCCTG TTGCTCGCG TCCCGGCCGC CGTCTACCGC 480
 10 CACCTGTGGA GGGACCGCGT ATGCCAGCTG TGCCACCCGT CGCCGGTCCA CGCCGCCGCC 540
 CACCTGAGCC TGGAGACTCT GACCGCTTTC GTGCTTCCTT TCGGGCTGAT GCTCGGCTGC 600
 TACACGTGA CGCTGGCACG GCTGCGGGGC GCCGCTGGG GCTCCGGGCG GCACGGGGCG 660
 CGGGTGGGCC GGCTGGTGAG CGCCATCGTG CTGCTCTCG GCTTGCTCTG GGCCCCCTAC 720
 CACGCAGTCA ACCTTCTGCA GGCGGTCGCA GCGCTGGCTC CACCGGAAGG GGCCTTGGCG 780
 15 AAGCTGGGCG GAGCCGGCCA GGCGGCGCA GCGGGAATA CGGCCTTGGC CTTCTTCAGT 840
 TCTAGCGTCA ACCCGGTGCT CTACGTCTTC ACCGCTGGAG ATCTGCTGCC CCGGCAGGT 900
 CCGCGTTTC TCACGCGGCT CTTCGAAGGC TCTGGGGAGG CCCGAGGGGG CGGCCGCTCT 960
 AGGGAAGGGA CCATGGAGCT CCGAACTACC CCTCAGCTGA AAGTGGTGGG GCAGGGCCGC 1020
 GGCAATGGAG ACCCGGGGGG TGGGATGGAG AAGGACGCTC CGGAATGGGA CCTTTGA 1077

20 (35) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 358 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

25 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Met Ser Val Cys Tyr Arg Pro Pro Gly Asn Glu Thr Leu Leu Ser Trp
 1 5 10 15

30 Lys Thr Ser Arg Ala Thr Gly Thr Ala Phe Leu Leu Leu Ala Ala Leu

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| | | | |
|----|---|-----|---------|
| | 20 | 25 | 30 |
| | Leu Gly Leu Pro Gly Asn Gly Phe Val Val Trp Ser Leu Ala Gly Trp | | |
| | 35 | 40 | 45 |
| 5 | Arg Pro Ala Arg Gly Arg Pro Leu Ala Ala Thr Leu Val Leu His Leu | | |
| | 50 | 55 | 60 |
| | Ala Leu Ala Asp Gly Ala Val Leu Leu Leu Thr Pro Leu Phe Val Ala | | |
| | 65 | 70 | 75 80 |
| | Phe Leu Thr Arg Gln Ala Trp Pro Leu Gly Gln Ala Gly Cys Lys Ala | | |
| | 85 | 90 | 95 |
| 10 | Val Tyr Tyr Val Cys Ala Leu Ser Met Tyr Ala Ser Val Leu Leu Thr | | |
| | 100 | 105 | 110 |
| | Gly Leu Leu Ser Leu Gln Arg Cys Leu Ala Val Thr Arg Pro Phe Leu | | |
| | 115 | 120 | 125 |
| 15 | Ala Pro Arg Leu Arg Ser Pro Ala Leu Ala Arg Arg Leu Leu Leu Ala | | |
| | 130 | 135 | 140 |
| | Val Trp Leu Ala Ala Leu Leu Leu Ala Val Pro Ala Ala Val Tyr Arg | | |
| | 145 | 150 | 155 160 |
| | His Leu Trp Arg Asp Arg Val Cys Gln Leu Cys His Pro Ser Pro Val | | |
| | 165 | 170 | 175 |
| 20 | His Ala Ala Ala His Leu Ser Leu Glu Thr Leu Thr Ala Phe Val Leu | | |
| | 180 | 185 | 190 |
| | Pro Phe Gly Leu Met Leu Gly Cys Tyr Ser Val Thr Leu Ala Arg Leu | | |
| | 195 | 200 | 205 |
| 25 | Arg Gly Ala Arg Trp Gly Ser Gly Arg His Gly Ala Arg Val Gly Arg | | |
| | 210 | 215 | 220 |
| | Leu Val Ser Ala Ile Val Leu Ala Phe Gly Leu Leu Trp Ala Pro Tyr | | |
| | 225 | 230 | 235 240 |
| | His Ala Val Asn Leu Leu Gln Ala Val Ala Ala Leu Ala Pro Pro Glu | | |
| | 245 | 250 | 255 |
| 30 | Gly Ala Leu Ala Lys Leu Gly Gly Ala Gly Gln Ala Ala Arg Ala Gly | | |
| | 260 | 265 | 270 |
| | Thr Thr Ala Leu Ala Phe Phe Ser Ser Ser Val Asn Pro Val Leu Tyr | | |
| | 275 | 280 | 285 |
| 35 | Val Phe Thr Ala Gly Asp Leu Leu Pro Arg Ala Gly Pro Arg Phe Leu | | |
| | 290 | 295 | 300 |
| | Thr Arg Leu Phe Glu Gly Ser Gly Glu Ala Arg Gly Gly Gly Arg Ser | | |
| | 305 | 310 | 315 320 |

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Arg Glu Gly Thr Met Glu Leu Arg Thr Thr Pro Gln Leu Lys Val Val
 325 330 335

Gly Gln Gly Arg Gly Asn Gly Asp Pro Gly Gly Gly Met Glu Lys Asp
 340 345 350

5 Gly Pro Glu Trp Asp Leu
 355

(36) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 1005 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

15 ATGCTGGGGA TCATGGCATG GAATGCAACT TGCAAAACT GGCTGGCAGC AGAGGCTGCC 60
 CTGGAAAAGT ACTACCTTTC CATTTTAT GGGATTGAGT TCGTTGTGGG AGTCCTTGGG 120
 AATACCATTG TTGTTTACGG CTACATCTTC TCTCTGAAGA ACTGGAACAG CAGTAATATT 180
 TATCTCTTTA ACCTCTCTGT CTCTGACTTA GCTTTTCTGT GCACCCTCCC CATGCTGATA 240
 AGGAGTTATG CCAATGGAAA CTGGATATAT GGAGACGTGC TCTGCATAAG CAACCGATAT 300
 20 GTGCTTCATG CCAACCTCTA TACCAGCATT CTCTTTCTCA CTTTATCAG CATAGATCGA 360
 TACTTGATAA TTAAGTATCC TTTCCGAGAA CACCTTCTGC AAAAGAAAGA GTTTGCTATT 420
 TTAATCTCCT TGGCCATTG GGTTTTAGTA ACCTTAGAGT TACTACCCAT ACTTCCCCTT 480
 ATAAATCCTG TTATAACTGA CAATGGCACC ACCTGTAATG ATTTTGCAAG TTCTGGAGAC 540
 CCCAACTACA ACCTCATTTA CAGCATGTGT CTAACACTGT TGGGGTTCCT TATCCTCTT 600
 25 TTTGTGATGT GTTCTTTTTA TTACAAGATT GCTCTCTTCC TAAAGCAGAG GAATAGGCAG 660
 GTTGCTACTG CTCTGCCCCT TGAAAAGCCT CTCAACTTGG TCATCATGGC AGTGGTAATC 720
 TTCTCTGTGC TTTTACACC CTATCACGTC ATGCGGAATG TGAGGATCGC TTCACGCCTG 780
 GGGAGTTGGA AGCAGTATCA GTGCACTCAG GTCGTCATCA ACTCCTTTTA CATGTGACA 840
 CGGCCTTTGG CCTTCTGAA CAGTGTATC AACCTGTCT TCTATTTTCT TTTGGGAGAT 900
 30 CACTTCAGGG ACATGCTGAT GAATCAACTG AGACACAACT TCAAATCCCT TACATCCTTT 960
 AGCAGATGGG CTCATGAACT CCTACTTTCA TTCAGAGAAA AGTGA -1005

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(37) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 334 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS:

(D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

10 Met Leu Gly Ile Met Ala Trp Asn Ala Thr Cys Lys Asn Trp Leu Ala
 1 5 10 15
 Ala Glu Ala Ala Leu Glu Lys Tyr Tyr Leu Ser Ile Phe Tyr Gly Ile
 20 25 30
 Glu Phe Val Val Gly Val Leu Gly Asn Thr Ile Val Val Tyr Gly Tyr
 35 40 45
 15 Ile Phe Ser Leu Lys Asn Trp Asn Ser Ser Asn Ile Tyr Leu Phe Asn
 50 55 60
 Leu Ser Val Ser Asp Leu Ala Phe Leu Cys Thr Leu Pro Met Leu Ile
 65 70 75 80
 20 Arg Ser Tyr Ala Asn Gly Asn Trp Ile Tyr Gly Asp Val Leu Cys Ile
 85 90 95
 Ser Asn Arg Tyr Val Leu His Ala Asn Leu Tyr Thr Ser Ile Leu Phe
 100 105 110
 Leu Thr Phe Ile Ser Ile Asp Arg Tyr Leu Ile Ile Lys Tyr Pro Phe
 115 120 125
 25 Arg Glu His Leu Leu Gln Lys Lys Glu Phe Ala Ile Leu Ile Ser Leu
 130 135 140
 Ala Ile Trp Val Leu Val Thr Leu Glu Leu Leu Pro Ile Leu Pro Leu
 145 150 155 160
 30 Ile Asn Pro Val Ile Thr Asp Asn Gly Thr Thr Cys Asn Asp Phe Ala
 165 170 175
 Ser Ser Gly Asp Pro Asn Tyr Asn Leu Ile Tyr Ser Met Cys Leu Thr
 180 185 190
 Leu Leu Gly Phe Leu Ile Pro Leu Phe Val Met Cys Phe Phe Tyr Tyr
 195 200 205
 35 Lys Ile Ala Leu Phe Leu Lys Gln Arg Asn Arg Gln Val Ala Thr Ala
 210 215 220

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Leu Pro Leu Glu Lys Pro Leu Asn Leu Val Ile Met Ala Val Val Ile
 225 230 235 240
 Phe Ser Val Leu Phe Thr Pro Tyr His Val Met Arg Asn Val Arg Ile
 245 250 255
 5 Ala Ser Arg Leu Gly Ser Trp Lys Gln Tyr Gln Cys Thr Gln Val Val
 260 265 270
 Ile Asn Ser Phe Tyr Ile Val Thr Arg Pro Leu Ala Phe Leu Asn Ser
 275 280 285
 10 Val Ile Asn Pro Val Phe Tyr Phe Leu Leu Gly Asp His Phe Arg Asp
 290 295 300
 Met Leu Met Asn Gln Leu Arg His Asn Phe Lys Ser Leu Thr Ser Phe
 305 310 315 320
 Ser Arg Trp Ala His Glu Leu Leu Leu Ser Phe Arg Glu Lys
 325 330

15 (38) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 1296 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

ATGCAGGCGC TTAACATTAC CCCGGAGCAG TTCTCTCGGC TGCTGCGGGA CCACAACCTG 60
 ACGGGGAGC AGTTCATCGC TCTGTACCGG CTGCGACCGC TCGTCTACAC CCCAGAGCTG 120
 25 CCGGGACGCG CCAAGCTGGC CCTCGTGCTC ACCGGCGTGC TCATCTTCGC CCTGGCGCTC 180
 TTTGGCAATG CTCTGGTGTT CTACGTGGTG ACCCGCAGCA AGGCCATGCG CACCGTCACC 240
 AACATCTTTA TCTGCTCCTT GCGCTCAGT GACCTGCTCA TCACCTTCTT CTGCATTCCC 300
 GTCACCATGC TCCAGAACAT TTCCGACAAC TGGCTGGGGG GTGCTTTCAT TTGCAAGATG 360
 GTGCCATTG TCCAGTCTAC CGCTGTTGTG ACAGAAATGC TCACTATGAC CTGCATTGCT 420
 30 GTGGAAAGGC ACCAGGGACT TGTGCATCCT TTTAAATGA AGTGGCAATA CACCAACCGA 480
 AGGGCTTTCA CAATGCTAGG TGTGGTCTGG CTGGTGGCAG TCATCGTAGG ATCACCCATG 540
 TGGCAGTGC AACAACTGA GATCAAATAT GACTTCCTAT ATGAAAAGGA ACACATCTGC 600
 TGCTTAGAAG AGTGGACCAG CCCTGTGCAC CAGAAGATCT ACACCACCTT CATCCTTGTO 660

ATCTCTTCC TCCTGCCTCT TATGGTGATG CTTATTCTGT ACAGTAAAAT TGGTTATGAA 720
 CTTTGGATAA AGAAAAGAGT TGGGGATGGT TCAGTGCTTC GAACTATTCA TGGAAAAGAA 780
 ATGTCCAAAA TAGCCAGGAA GAAGAAACGA GCTGTCATTA TGATGGTGAC AGTGGTGGCT 840
 CTCCTTGCTG TGTGCTGGGC ACCATTCCAT GTTGTCATA TGATGATTGA ATACAGTAAT 900
 5 TTTGAAAAGG AATATGATGA TGTCACAATC AAGATGATTT TTGCTATCGT GCAAATTATT 960
 GGATTTTCCA ACTCCATCTG TAATCCCATT GTCTATGCAT TTATGAATGA AAACCTTCTC TCCAGCACAA1020
 AAAAAATGTTT TGTCTGCAGT TTGTTATTGC ATAGTAAATA AAACCTTCTC TCCAGCACAA1080
 AGGCATGGAA ATTCAGGAAT TACAATGATG CGGAAGAAAG CAAAGTTTTC CCTCAGAGAG1140
 AATCCAGTGG AGGAAACCAA AGGAGAAGCA TTCAGTGATG GCAACATTGA AGTCAAATTG1200
 10 TGTGAACAGA CAGAGGAGAA GAAAAAGCTC AAACGACATC TTGCTCTCTT TAGGTCTGAA1260
 CTGGCTGAGA ATTCTCCTTT AGACAGTGGG CATTAA 1296

(39) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 431 amino acids
 (B) TYPE: amino acid
 (C) STRANDEDNESS:
 (D) TOPOLOGY: not relevant

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

20 Met Gln Ala Leu Asn Ile Thr Pro Glu Gln Phe Ser Arg Leu Leu Arg
 1 5 10 15
 Asp His Asn Leu Thr Arg Glu Gln Phe Ile Ala Leu Tyr Arg Leu Arg
 20 25 30
 25 Pro Leu Val Tyr Thr Pro Glu Leu Pro Gly Arg Ala Lys Leu Ala Leu
 35 40 45
 Val Leu Thr Gly Val Leu Ile Phe Ala Leu Ala Leu Phe Gly Asn Ala
 50 55 60
 Leu Val Phe Tyr Val Val Thr Arg Ser Lys Ala Met Arg Thr Val Thr
 65 70 75 80
 30 Asn Ile Phe Ile Cys Ser Leu Ala Leu Ser Asp Leu Leu Ile Thr Phe
 85 90 95
 Phe Cys Ile Pro Val Thr Met Leu Gln Asn Ile Ser Asp Asn Trp Leu

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| | 100 | 105 | 110 |
|----|--|-----|-----|
| | Gly Gly Ala Phe Ile Cys Lys Met Val Pro Phe Val Gln Ser Thr Ala 115 120 125 | | |
| 5 | Val Val Thr Glu Met Leu Thr Met Thr Cys Ile Ala Val Glu Arg His 130 135 140 | | |
| | Gln Gly Leu Val His Pro Phe Lys Met Lys Trp Gln Tyr Thr Asn Arg 145 150 155 160 | | |
| | Arg Ala Phe Thr Met Leu Gly Val Val Trp Leu Val Ala Val Ile Val 165 170 175 | | |
| 10 | Gly Ser Pro Met Trp His Val Gln Gln Leu Glu Ile Lys Tyr Asp Phe 180 185 190 | | |
| | Leu Tyr Glu Lys Glu His Ile Cys Cys Leu Glu Glu Trp Thr Ser Pro 195 200 205 | | |
| 15 | Val His Gln Lys Ile Tyr Thr Thr Phe Ile Leu Val Ile Leu Phe Leu 210 215 220 | | |
| | Leu Pro Leu Met Val Met Leu Ile Leu Tyr Ser Lys Ile Gly Tyr Glu 225 230 235 240 | | |
| | Leu Trp Ile Lys Lys Arg Val Gly Asp Gly Ser Val Leu Arg Thr Ile 245 250 255 | | |
| 20 | His Gly Lys Glu Met Ser Lys Ile Ala Arg Lys Lys Lys Arg Ala Val 260 265 270 | | |
| | Ile Met Met Val Thr Val Val Ala Leu Phe Ala Val Cys Trp Ala Pro 275 280 285 | | |
| 25 | Phe His Val Val His Met Met Ile Glu Tyr Ser Asn Phe Glu Lys Glu 290 295 300 | | |
| | Tyr Asp Asp Val Thr Ile Lys Met Ile Phe Ala Ile Val Gln Ile Ile 305 310 315 320 | | |
| | Gly Phe Ser Asn Ser Ile Cys Asn Pro Ile Val Tyr Ala Phe Met Asn 325 330 335 | | |
| 30 | Glu Asn Phe Lys Lys Asn Val Leu Ser Ala Val Cys Tyr Cys Ile Val 340 345 350 | | |
| | Asn Lys Thr Phe Ser Pro Ala Gln Arg His Gly Asn Ser Gly Ile Thr 355 360 365 | | |
| 35 | Met Met Arg Lys Lys Ala Lys Phe Ser Leu Arg Glu Asn Pro Val Glu 370 375 380 | | |
| | Glu Thr Lys Gly Glu Ala Phe Ser Asp Gly Asn Ile Glu Val Lys Leu 385 390 395 400 | | |

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Cys Glu Gln Thr Glu Glu Lys Lys Lys Leu Lys Arg His Leu Ala Leu
405 410 415

Phe Arg Ser Glu Leu Ala Glu Asn Ser Pro Leu Asp Ser Gly His
420 425 430 --

5 (40) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:

- 10 (A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

CTGTGTACAG CAGTTCGCAG AGTG

24

(41) INFORMATION FOR SEQ ID NO:40:

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

GAGTGCCAGG CAGAGCAGGT AGAC

24

(42) INFORMATION FOR SEQ ID NO:41:

25 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 31 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

CCCGAATTCC TGCTTGCTCC CAGCTTGCC C

31

(43) INFORMATION FOR SEQ ID NO:42:

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- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 32 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
5 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

TGTGGATCCT GCTGTCAAAG GTCCCATTCG GG

32

10 (44) INFORMATION FOR SEQ ID NO:43:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 20 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
15 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

TCACAATGCT AGGTGTGGTC

20

20 (45) INFORMATION FOR SEQ ID NO:44:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
25 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

TGCATAGACA ATGGGATTAC AG

22

30 (46) INFORMATION FOR SEQ ID NO:45:

- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 511 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single

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(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

TCACAATGCT AGGTGTGGTC TGGCTGGTGG CAGTCATCGT AGGATCACCC ATGTGGCAGC 60
5 TGCAACAAC TGAATCAAA TATGACTTCC TATATGAAAA GGAACACATC TGCTGCTTAG 120
AAGAGTGGAC CAGCCCTGTG CACCAGAAGA TCTACACCAC CTTTCATCCTT GTCATCCTCT 180
TCCTCCTGCC TCTTATGGTG ATGCTTATTC TGTACGTAAA ATTGGTTATG AACCTTGGAT 240
AAAGAAAAGA GTTGGGGATG GTTCAGTGCT TCGAACTATT CATGGAAAAG AAATGTCCAA 300
AATAGCCAGG AAGAAGAAAC GAGCTGTCTAT TATGATGGTG ACAGTGGTGG CTCTCTTTC 360
10 TGTGTGCTGG GCACCATTC ATGTTGTCCA TATGATGATT GAATACAGTA ATTTTGAAAA 420
GGAATATGAT GATGTCACAA TCAAGATGAT TTTTGCTATC GTGCAAATTA TTGGATTTC 480
CAACTCCATC TGTAATCCCA TTGTCTATGC A 511

(47) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

CTGCTTAGAA GAGTGGACCA G

21

(48) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (iv) ANTI-SENSE: NO

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

CTGTGCACCA GAAGATCTAC AC

22

(49) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

CAAGGATGAA GGTGGTGTAG A

21

(50) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

GTGTAGATCT TCTGGTGAC AGG

23

(51) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

GCAATGCAGG TCATAGTGAG C

21

(52) INFORMATION FOR SEQ ID NO:51:

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- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
5 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: YES
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:
10 TGGAGCATGG TGACGGGAAT GCAGAAG 27
- (53) INFORMATION FOR SEQ ID NO:52:
- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 27 base pairs
 (B) TYPE: nucleic acid
15 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iv) ANTI-SENSE: YES
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:
20 GTGATGAGCA GGTCACTGAG CGCCAAG 27
- (54) INFORMATION FOR SEQ ID NO:53:
- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 23 base pairs
 (B) TYPE: nucleic acid
25 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic)
- (iv) ANTI-SENSE: NO
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:
30 GCAATGCAGG CGCTTAACAT TAC 23
- (55) INFORMATION FOR SEQ ID NO:54:
- (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 22 base pairs

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- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

5 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

TTGGGTTACA ATCTGAAGGG CA

22

(56) INFORMATION FOR SEQ ID NO:55:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 23 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

10

(ii) MOLECULE TYPE: DNA (genomic)

15 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

ACTCCGTGTC CAGCAGGACT CTG

23

(57) INFORMATION FOR SEQ ID NO:56:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: DNA (genomic)

25 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

TGCGTGTTC TGGACCCTCA CGTG

24

(58) INFORMATION FOR SEQ ID NO:57:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 29 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

30

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(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

CAGGCCTTGG ATTTTAATGT CAGGGATGG

29

5 (59) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

GGAGAGTCAG CTCTGAAAGA ATTCAGG

27

15 (60) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

TGATGTGATG CCAGATACTA ATAGCAC

27

25 (61) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 27 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

CCTGATTCAT TTAGGTGAGA TTGAGAC

27

(62) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

GACAGGTACC TTGCCATCAA G

21

(63) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

20 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

CTGCACAATG CCAGTGATAA GG

22

(64) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

30 (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

CTGACTTCTT GTTCCTGGCA GCAGCGG

27

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(65) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 27 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

10 AGACCAGCCA GGGCACGCTG AAGAGTG

27

(66) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 32 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

20 GATCAAGCTT CCATCCTACT GAAACCATGG TC

32

(67) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:

- 25 (A) LENGTH: 35 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

30 GATCAGATCT CAGTTCCAAT ATTCACACCA CCGTC

35

(68) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 22 base pairs
- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: single
- (D) TOPOLOGY: linear

- 5 (ii) MOLECULE TYPE: DNA (genomic)
- (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

CTGGTGTGCT CCATGGCATC CC

22

(69) INFORMATION FOR SEQ ID NO:68:

- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 22 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- 15 (ii) MOLECULE TYPE: DNA (genomic)
- (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

GTAAGCCTCC CAGAACGAGA GG

22

(70) INFORMATION FOR SEQ ID NO:69:

- 20 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

- 25 (ii) MOLECULE TYPE: DNA (genomic)
- (iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

CAGCGCAGGG TGAAGCCTGA GAGC

24

(71) INFORMATION FOR SEQ ID NO:70:

- 30 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 24 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear

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(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

GGCACCTGCT GTGACCTGTG CAGG

24

5 (72) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

10 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

GTCCTGCCAC TTCGAGACAT GG

22

15 (73) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

20 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

GAAACTTCTC TGCCCTTACC GTC

23

25 (74) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 base pairs

(B) TYPE: nucleic acid

(C) STRANDEDNESS: single

30 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(iv) ANTI-SENSE: NO

- 60 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

CCAACACCAG CATCCATGGC ATCAAG

26

(75) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:

- 5 (A) LENGTH: 27 base pairs
 (B) TYPE: nucleic acid
 (C) STRANDEDNESS: single
 (D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

10 (iv) ANTI-SENSE: YES

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

GGAGAGTCAG CTCTGAAAGA ATTCAGG

27